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CONTENTS OF PREVIOUS NUMBER

OCTOBER 1943. NUMBER 4

A Caution Against Too Liberal Use of Citrated Blood in Transfusions. Jacques Bruneau, M.D., and Evarts A. Graham, M.D., St. Louis.

Effects of Morphine in Experimental Shock Due to Hemorrhage. Alfred Blalock, M.D., Baltimore.

Arterial Blood Supply of the Breast: Revised Anatomic Data Relating to Reconstructive Surgery. Jacques W. Maliniac, M.D., New York.

Adventitious Bursas. Ronald M. Buck, M.D.; John R. McDonald, M.D., and Ralph K. Ghormley, M.D., Rochester, Minn.

Effect of Sulfathiazole Administered Orally and Sulfanilamide Implanted Locally on Contaminated Wounds: Experimental Study. Jere W. Lord Jr., M.D.; Arthur H. Blakemore, M.D., and Paul L. Stefko, New York.

Hemangioma of the Synovial Membrane of the Knee Joint Cured by Synovectomy. Paul H. Harmon, M.D., Ph.D., Sayre, Pa.

Spontaneous Closure of an Arteriovenous Fistula: Report of a Case. Robert F. Barber, M.D., Brooklyn, and Captain John L. Madden, Medical Corps, Army of the United States.

Role of the Chemical Laboratory in Diagnosis of Neoplastic Diseases of Bone. Helen Quincy Woodard, Ph.D., New York.

Progress in Orthopedic Surgery for 1942: A Review Prepared by an Editorial Board of the American Academy of Orthopaedic Surgery (To Be Continued).

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VOLUME 47 NOVEMBER 1943 NUMBER 5

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HISTOMECHANICAL ANALYSIS OF NERVE REUNION IN THE RAT AFTER TUBULAR SPLICING

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CHICAGO

The purpose of studying repair of nerves in experimental animals, such as the rat, is to perform model experiments in which the phenomena inaccessible to large scale investigation in human subjects may be analyzed under controlled conditions. It is neither intended nor to be expected that the results obtained in such model experiments will become immediately applicable for clinical use. What is to be expected, however, is that the lessons learned from those experiments, when properly interpreted in terms of the conditions prevailing in the human body, may furnish directives for clinical research and possibly clinical practice. In a preceding article [1] a method of reuniting severed nerves by means of arterial cuffs was outlined, and the superior results of nerve regeneration following "sleeve splicing" were described. Since that publication, the method has proved its value on several hundred experimental animals, including rats, chickens, rabbits, cats and monkeys. We have gained from these studies much information about the prerequisites of nerve regeneration; above all, insight into the reasons for the success of the sleeve-splicing method. While it would be idle to predict whether or not the arterial sleeve will make a suitable link in human nerves, the lessons which we have learned from analyzing the mechanism of its action in animals are of such a general and fundamental nature that they may well be heeded in whatever method one may elect to follow in surgical practice. These lessons pertain particularly to the early stages of regeneration. As will be shown in this paper, the whole course of nerve regeneration is essentially decided within a matter of days or, at best, weeks after the nerve union. Most of the processes thereafter are determined by the conditions laid down during the initial phase of regeneration, and the prospects of eventual nerve restoration will benefit or suffer, depending on the success or the failure of the early union.

It is with these facts in mind that we present in this article an analysis of the events following sleeve splicing and an evaluation of their significance for successful nerve regeneration. Some of these phenomena are common to all kinds of nerve reunion, and others are peculiar to the sleeve-splicing technic. Some of the latter

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1. Weiss, P.: Nerve Regeneration in Rat Following Tubular Splicing of Severed Nerves, Arch. Surg. **46**:525-547 (April) 1943.

are shared by other tubulation methods. In fact, Kirk and Lewis [2] in their excellent histologic study of nerve regeneration after fascial tubulization have noticed some of the phenomena emphasized by our studies. In the preceding study, the multiple functions of the arterial sleeve in facilitating nerve regeneration have been listed. These functions include insurance of straight and unbranched nerve fiber outgrowth, and prevention of escape of fibers, of invasion of connective tissue and of formation of fibrotic and growth-obstructing suture lines. The present study will furnish an account of how these functions are being exercised.

EXPERIMENTAL STUDY

MATERIAL AND METHOD

Our results are based on a study of 39 rat nerves, either tibial or peroneal, which were transected, reunited by means of an arterial sleeve and then studied between one and fifteen days after the operation. In general, the procedure described in the previous article [1] was followed. The arterial sleeves were so chosen as to fit comfortably over the nerve ends without producing constrictions. The ends of the nerves were not closely apposed but were left separated by a gap varying in extent from a fraction of to several times the diameter of the nerve, i. e., from about five-tenths to several millimeters. In some cases the gap became wider than was intended, owing to the partial retraction of one or both nerve stumps from the sleeve. In contrast to our earlier procedure, excess blood was not blotted from the interior of the gap but was left in place. This blood played an integral part in the healing process not formerly realized in its full meaning. As anesthesia induced with soluble pentobarbital U. S. P. was maintained for several hours, the seal between the nerve ends had become sufficiently firm by the time the animals resumed movement.

In order to investigate the phenomena taking place at the distal suture line of a graft in the absence of nerve fibers, splices between two peripheral nerve segments were effected. For this purpose, a piece several millimeters in length was excised from the proximal sciatic nerve. Two weeks was then allowed for the degeneration of the peripheral stump. After this period either the tibial or the peroneal nerve or both were transected and reunited by arterial sleeves. In this case neither stump contained intact nerve fibers, and such nerves will be referred to henceforth as "aneuritic." In 8 animals, simple biopsies of the union were made within two weeks after the operation, with special attention to the medium filling the sleeves between the nerve ends. The biopsy specimens from the remaining 31 nerves were straightened on cardboard, fixed in Bouin's solution, embedded in paraffin, sectioned serially at 10 microns and impregnated with silver according to Bodian, with an additional Mallory triple azan stain for the differentiation of connective tissue superimposed on the silver stain in sections selected at regular intervals. In all illustrations the proximodistal direction of the nerve is from bottom to top.

GENERAL RESULTS

Immediately after the operation, the artery is attached to the nerve ends by clotted blood and lymph. The gap between the nerve ends is filled with a dark purple blood clot visible through the translucent walls of the artery. This filling and the moderate tension along the nerve keep the arterial tubes from collapsing. Within four to five days after the operation the blood clot undergoes profound physical and chemical transformations. It is through these transformations that the severed texture of the nerve becomes rewoven in such a manner as to prepare the unimpeded transit of sheath cells and regenerating axons from one stump to the other. These changes are diagrammatically summarized in figure 1, representing the situation on the first, third and fifth days. Resolved into component steps, the reweaving process occurs as follows:

Phase 1.—Immediately after the operation, a firm connection between the nerve ends is established by the fibrin reticulum of the clotting blood in the gap, the fibrin threads inserting directly on the cut surfaces. The erythrocytes lie in clusters embedded in the fibrin meshes (fig. 1 *A*).

2. Kirk, E. G., and Lewis, D. D.: Regeneration in Peripheral Nerves, Bull. Johns Hopkins Hosp. **28**:71-80, 1917.

Phase 2.—Within twenty-four hours most of the erythrocytes disintegrate, while the fibrin framework persists. Later proteolysis along the inner wall of the artery breaks the connections between the clot and the sleeve. Thus detached all around its circumference, while firmly cemented to the two nerve stumps, the cylindric clot becomes subjected to longitudinal tension.

Phase 3.—The fibrin net assumes preponderantly longitudinal orientation corresponding to the lines of tension (fig. 1 *B*).

Phase 4.—By the third day, fibrinolytic liquefaction has set in within the clot. Its action is differential in that it dissolves mostly the transverse threads of the fibrin meshes while sparing the longitudinal ones (fig. 1 *B*). Somehow tension has rendered the longitudinally oriented fibrin fibers more resistant to proteolytic destruction.

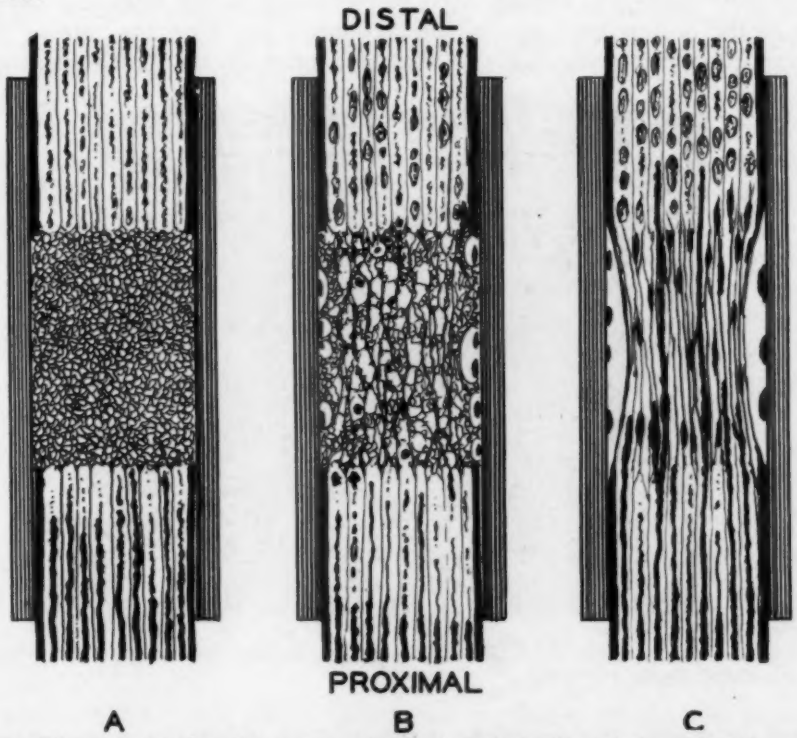

Fig. 1.—Diagram showing three stages in the transformation of the union tissue between sleeve-spliced nerve stumps, one (*A*), three (*B*) and five (*C*) days after the operation.

Phase 5.—By this time migration of cells into the region of the former gap has begun. Sheath cells and nerve fibers move out along the solid strands of fibrin and hence are likewise oriented in the longitudinal direction of the nerve. Simultaneously, macrophages move in and continue to clear the spaces between the fibers.

Phase 6.—By the fifth day, a continuous, straight cell bridge, followed by regenerating axons, extends across the former gap (fig. 1 *C*). The Schwann cells of this bridge stimulate the deposition of collagen along their surfaces, and a system of collagen fibers, oriented longitudinally, is laid down as the endoneurium of the nerve segment.

Phase 7.—When continuity between the nerve stumps is completely restored, channels are opened for the passage of endoneurial fluid, which may serve to keep the interior of the nerve in the required state of fluidity.

Comment.—This survey shows that the interweaving of severed nerve stumps occurs essentially by three successive processes: (1) the formation of an oriented scaffolding of fibrin fibers; (2) an oriented migration of living cells and nerve fibers, retracing and populating the fibrin matrix, and (3) a collagenization under the influence of these cells of the intercellular spaces in continuity with the stumps. By contrast, the scar forming between two nerve ends not protected by a sleeve fails to undergo longitudinal orientation, becomes invaded by all kinds of surrounding connective tissue cells and establishes a sort of foreign block in the continuity of the nerve. The two stumps, instead of being rewoven into an integral fabric over which sheath cells, nerve fibers, blood vessels and capillary liquid may pass freely and easily, are merely patched up by what amounts to a mechanical cementing tissue of low permeability.

These differences will become even more evident in the following day by day account of the healing progress. This account is based on the rate of progress as observed in the average case. While the timing varies slightly, depending on

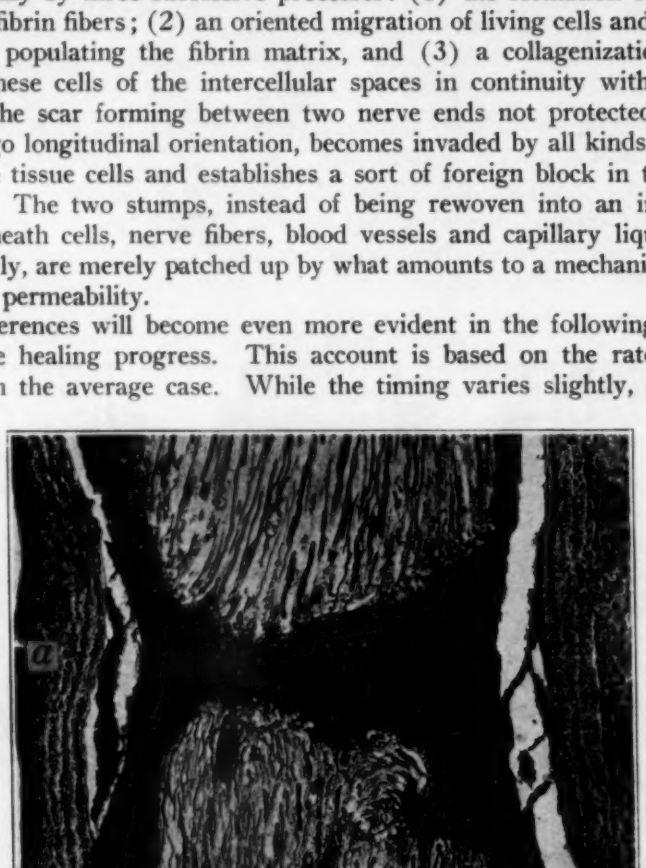

Fig. 2.—Union by blood clot of sleeve-spliced nerve stumps, one day after the operation; *a*, wall of arterial sleeve (× 120).

the age of the animal, the size of the nerves and the length of the gap, the fluctuations affect only the onset and duration, but not the order of succession, of the listed steps. For convenience, we shall designate the tissue filling the gap and reuniting the nerve stumps as the "union tissue," the term to be applied through all stages of transformation, beginning with the early blood clot and terminating with the restoration of the new nerve segment.

ONE DAY

Figure 2 shows the condition of the union after twenty-four hours. Degeneration of the axons in the peripheral stump has set in and some ovoids can be seen near the cut. Most axons are still intact, as it has been generally observed that wallerian degeneration within the sleeve is somewhat retarded, presumably owing to slight compression.[3] One notices in the picture that the two stumps are cemented

3. Weiss, P., and Davis, H.: Pressure Block in Nerves Provided with Arterial Sleeves. J. Neurophysiol. **8**:269-286, 1943.

by a blood clot firmly adherent to the cut surfaces. In contrast, there is a gap between the nerve and the arterial wall. This gap is an artefact resulting from the shrinkage of the preparation during fixation. However, the fact that this detachment has occurred along the arterial wall indicates that the clot does not adhere firmly to the artery, although its link with the two nerves is solid. The lack of firm ties between nerve and sleeve reduces, of course, the holding strength of the latter. On the other hand, we have regularly observed that the slipping out of the nerve ends from the sleeve is counteracted by the suction which such withdrawal would necessarily exert. With the sleeve gripping the surface of the nerve closely, the nerves act like the plungers in the barrel of a syringe; i. e., they could not be separated without creating a vacuum in between, and the suction of this vacuum helps to keep them in place as long as the pull remains moderate.

After the blood between the stumps has become clotted, it strengthens the formerly tenuous union between the nerve stumps. Blood in an otherwise empty artery, as one knows, would long remain liquid. In our arterial cuffs, tissue juice and exudates of the nerve ends obviously inhibit the antithrombic action of the artery. The

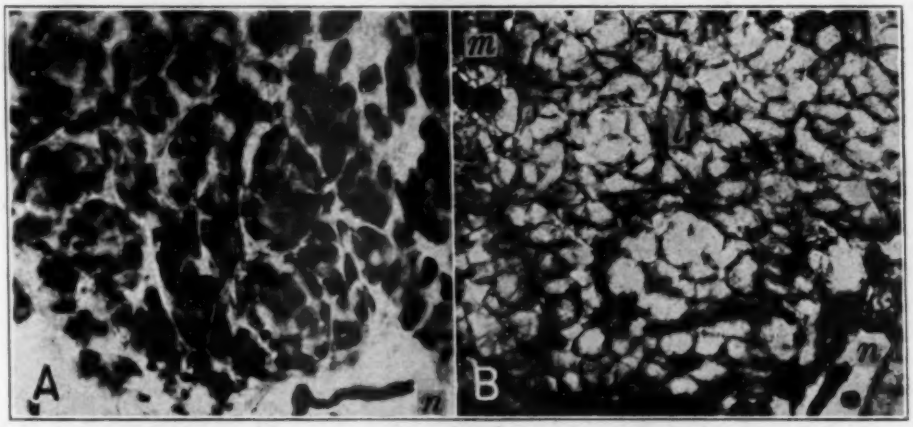

Fig. 3.—*A*, part of the union tissue of figure 2 under high magnification (× 630); erythrocytes dark, fibrin framework light; *n*, cut end of an axon. *B*, union tissue early on the second day (× 630); *n*, end of a cut nerve fiber; *m*, macrophage; *l*, leukocyte.

firmest attachment between artery and nerve is effected at the two ends of the artery where epineurial connective tissue grows over the sleeve, incorporating it in the continuity of the nerve. Under high magnification, the clot can be seen to be composed of small groups of erythrocytes, densely packed, lying in the meshes of a fibrin network (fig. 3*A*).

TWO DAYS

Biopsy on the second day already reveals the presence of a liquid menstruum inside of the sleeve composed, evidently, in part of serum oozing from the clot owing to syneresis, and in part of liquids released by the progressive destruction of the red cells and the liquefaction of fibrin. The fluid is still dark colored. More details can be seen in the histologic pictures. As in the one day preparations, the solid parts of the matrix are firmly cemented to the nerve ends but adhere only lightly to the wall of the artery. The red cells have mostly disintegrated, although their ghosts are still intact. Inspection under high magnification (fig. 3*B*) reveals the presence of a fine honeycomb of fibrin, the meshes of which are the spaces formerly occupied by the red blood corpuscles. The disappearance of the red cells

enables the white blood cells to stand out in the pictures. They consist of granular leukocytes, some lymphocytes and only an occasional macrophage. A sample count indicated about 3,000 of the larger leukocytes per cubic millimeter within the clot. There is a denser accumulation of these cells along the arterial wall, where many of them can be seen to liquefy the surrounding clot. Thus vacuoles appear in the clot all along its surface, each vacuole the product of a single cell. On becoming confluent, these vacuoles form a liquid layer, separating the clot from the artery. Figure 4 shows this process well advanced on the third day. Thus, while the clot from the beginning has failed to become sealed to the artery, it is now actively detached from it by this surface liquefaction.

This has a decided influence on the tensional pattern within the union tissue. The origin of these tensions is twofold. If the nerve ends tend to retract, they

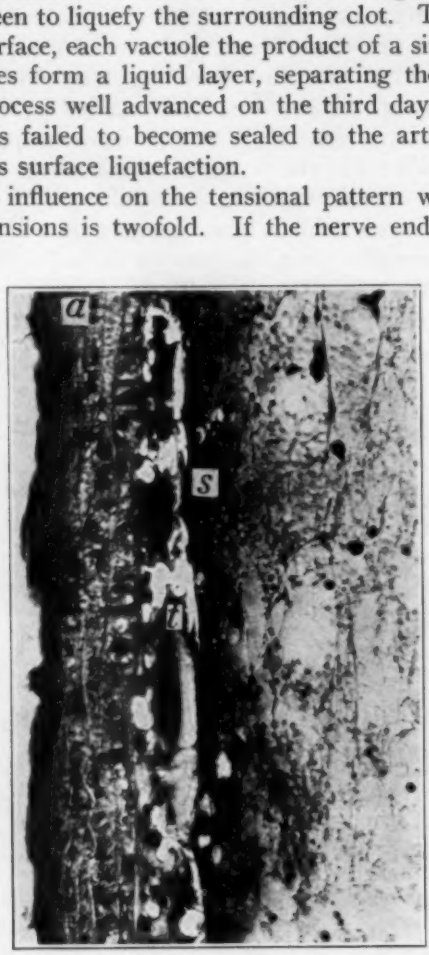

Fig. 4.—Proteolytic detachment of the union tissue from the arterial wall; note confluent cavities around liquefying cells; *a*, sleeve wall; *s*, condensed surface of clot; *t*, liquefied space between *a* and *s* (× 240).

put the intervening clot under elastic strain oriented longitudinally along the axis of the nerve. However, even in the absence of such extraneous pull, tensions arise within the clot owing to its syneresis. This syneresis, which is due to the progressive segregation of the solid from the liquid phases of the colloids of the clot, will contract the clot in those directions in which shrinkage is possible, i. e., where the surface of the clot is free. However, where it is attached internal tensions will arise between the points or surfaces of attachment. These elastic tensions will equal the force that would have to be exerted if the clot had first been allowed to shrink unimpeded and then been returned to the former length by actual stretching. Since the clot in all our cases is essentially a cylinder, attached at its base and top to the nerve stumps while free along its mantle, syneresis will lead to actual shrinkage

in the radial directions but to the setting up of elastic tensions in the longitudinal direction along which yielding is precluded by the resistance of the nerve ends.

In accordance with this tensional pattern, the fibrin framework, beginning with the second day, assumes a striking longitudinal organization (fig. 5 *A*), which, in view of the known orienting action of tension on the arrangement of fibrin fibrils, can be directly ascribed to the mechanical stresses in the clot. Concurrently with the increasing prominence of the longitudinal fibrin aggregates, a dissolution of the fibrin braces oriented otherwise than longitudinally takes place. Thus, the longitudinal parts of the fibrin network are strengthened while the nonlongitudinal ones are resorbed by proteolysis. Though this liquefaction is often more marked at first near the ends of the nerves, it likewise arises in many places in the interior of the clot more or less simultaneously. It results in a gradual increase in the size

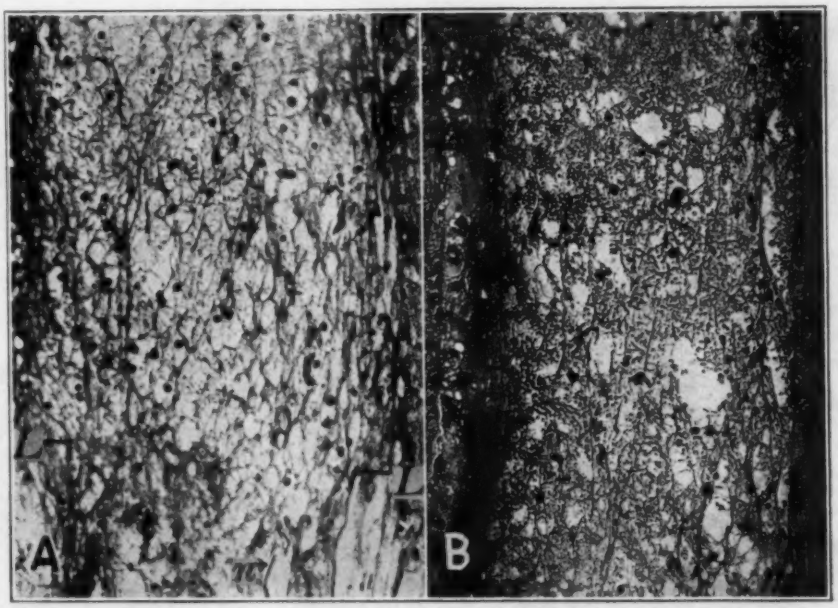

Fig. 5.—*A*, transition from proximal stump to union tissue late on second day. Heavy fibrin fibers begin to appear in the longitudinal direction (lines of tension). Note scattered leukocytes and macrophages and liquefying activity of the latter (cavities) in the denser outer parts of the clot. *L-L*, level of transection, containing the ends of cut nerve fibers (*n*) (× 230). *B*, union tissue on the third day. Note the destruction of the fibrin net, exempting the longitudinal strands (× 120).

of the individual meshes, more and more of the meshes of the original honeycomb becoming confluent as the partitions are dissolved.

THREE DAYS

By the third day, the condition illustrated in figure 5 *B* is reached. Only the gap region, measuring several millimeters, is shown in the picture. One can see the lumen of the sleeve filled with a spongy mass consisting, according to its staining reaction, of fibrin. These are the ruins, as it were, of the original compact clot. Liquefaction along the wall of the sleeve has become very extensive, and so has the consequent detachment of the union tissue from the arterial wall. Large liquid spaces pervade the clot. The longitudinal fibrin strands have become even heavier

and straighter, and many extend throughout the clot. Viewed at higher magnification, the details of the transformation of the clot become evident (fig. 6*A*). In some places, the outline of the original honeycomb of fibrin around red cell ghosts can still be seen, but most of the meshes have widened considerably, with marked elongation in the direction of the nerve. The heavier, longitudinal fibrin strands are clearly visible (compare also fig. 4), but they are still interconnected by cross links. As one can see from the picture, cells are still very scarce in the central portions of the union tissue. Near the nerve ends, however, cell migration has set in, as will be discussed presently. The longitudinal fibrin fibers are from their very first appearance anchored in the two cut surfaces of the nerve. This is already clear on the second day (fig. 5*A*) but is even more marked on the third day. As the nerve fiber substance near the wound is at this stage liquid, the solid frame of the cut surface of the nerve consists of the rims of the neurilemmal tubes and

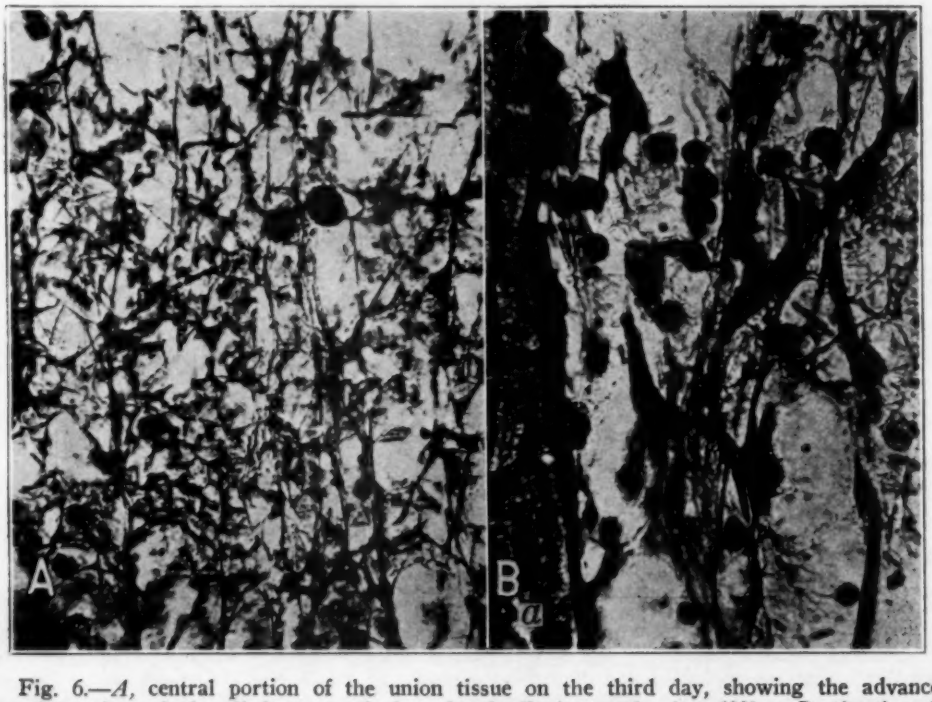

Fig. 6.—*A*, central portion of the union tissue on the third day, showing the advanced transformation of the fibrin network into longitudinal strands (× 630). *B*, sheath cells (spindle-shaped) on the third day, climbing along the fibrin network; *a*, sleeve wall (× 630).

the endoneural collagen. It is only along these solid lines that fibrin fibers can insert. Therefore, the fibrin framework forms in direct continuation of the architecture of the nerve stumps.

The degree of cell invasion observed at the end of the third day varies greatly among different cases. While in some the union tissue may not contain more than a few isolated Schwann cells, in others some strands of such cells may have moved clear across and reached the opposite stump. In practically all cases, however, the invasion from the cut surfaces has started on a broad front. The outgrowing sheath cells (fig. 6*B*) move definitely as single, slender, spindle-shaped cells with far drawn out ends,[2] staining heavily with silver.[4] Several sheath cells may follow

4. Holmes, W., and Young, J. Z.: Nerve Regeneration After Immediate and Delayed Suture, J. Anat. **77**:63-96, 1942.

each other in tandem arrangement, but they do not, at this stage, offer the appearance of those smoothly contoured Schwann bands seen during later phases. The sheath cells can be seen to move without exception along the heavy fibrin fibers of the union tissue. While there are still some transverse fibrin connections, sheath cells may follow them to cross from one strand to another, as seen in figure 6*B*. However, such deviations are temporary and cease with the gradual breakdown of the fibrin cross links. Sheath cell migration proceeds from both nerve stumps. The presence of a noncellular "no man's land" between the stumps in our cases has permitted us to establish this point with certainty.

Along with the sheath cells, macrophages appear in the region near the wound. Since these macrophages have not previously been present in the interior of the clot in such numbers, it is evident that most of them have come from the nerve. They may be mobilized cells of the endoneurial tissue. Theoretically, there is a possibility that some of them may be transformed sheath cells. One of us (P. W.) has recently observed the transformation of sheath cells into cells of the macrophage type in tissue cultures of embryonic chick ganglions. However, whether this can also occur in the body remains to be demonstrated, and nothing we have thus far seen suggests this possibility. Macrophages seen after nerve section are usually described as engaged in a one way traffic into the nerve fibers. Yet our present observations prove that numbers of them move in the opposite direction, i. e., from the nerve into the union tissue. Their relatively late appearance on the scene disqualifies them as the primary agents of proteolysis. Liquefaction is well under way before they arrive in larger numbers. On the other hand, once present, they participate in the proteolytic activity and dissolve the remaining fibrin threads in their way. Again, as in the preceding phase, the longitudinally oriented fibrin fibers resist this dissolution.

FOUR DAYS

The fourth day brings merely an elaboration of the phenomena observed on the third day, with both the straightening of the union tissue and the immigration of cells into it progressing rapidly. Moreover, formation of new blood vessels and the outgrowth of regenerating axons are becoming more conspicuous. Well formed blood vessels can be seen to traverse the scar as early as on the third day, but more frequently on the fourth day. Significantly, these vessels arise as direct continuations of the vessels of the proximal and distal stumps and course in the longitudinal direction without much branching. This contrasts with the vascularization of an ordinary suture scar, into which the blood vessels penetrate from the epineurial and extraneural spaces (fig. 11*A*). Apparently the regenerating blood vessels, like the other components of the regenerating nerve, are guided by the fibrin architecture of the union tissue. A well oriented union tissue thus insures straight vascular reconnection between proximal and peripheral stumps.

Most of the axons of the peripheral stump have, in the meantime, disintegrated. In the proximal stump, the initial retrograde changes near the wound have been superseded by axon regeneration. Many of the new sprouts have arrived at the old level of the cross section and have proceeded into the union tissue. In doing so, they follow the same longitudinal guide lines as the sheath cells. The relative simplicity and clarity of the conditions in the clot make these cases favorable objects for the study of the relation between regenerating sprouts and sheath cells. As a general result of many observations on such preparations, we have become convinced that the vast majority of newly sprouting axons is closely associated with sheath cells. Contact need not exist over the full length of the axon, at least not during the earlier

phases. Some stretches may be bare, much as they are in early development.[5] This fact makes it difficult to decide whether there are any sprouts that travel in complete independence of sheath cells. That they can do so for a certain distance is evident in our preparations. It is equally clear, however, that such bareness is the exception rather than the rule.[6]

Some branching of the outgrowing sprouts does occur at nodal points of the fibrin network. However, such branching remains on a minor scale. Also most of the side branches are abortive, particularly those that do not run longitudinally. Presumably as the cross links among the longitudinal fibrin threads are progressively resorbed, nerve fibers which happen to have started to grow out along them are being deprived of their support and are then likewise reduced. This process soon leaves only those nerve fibers in the field which have grown out straight and essentially unbranched.

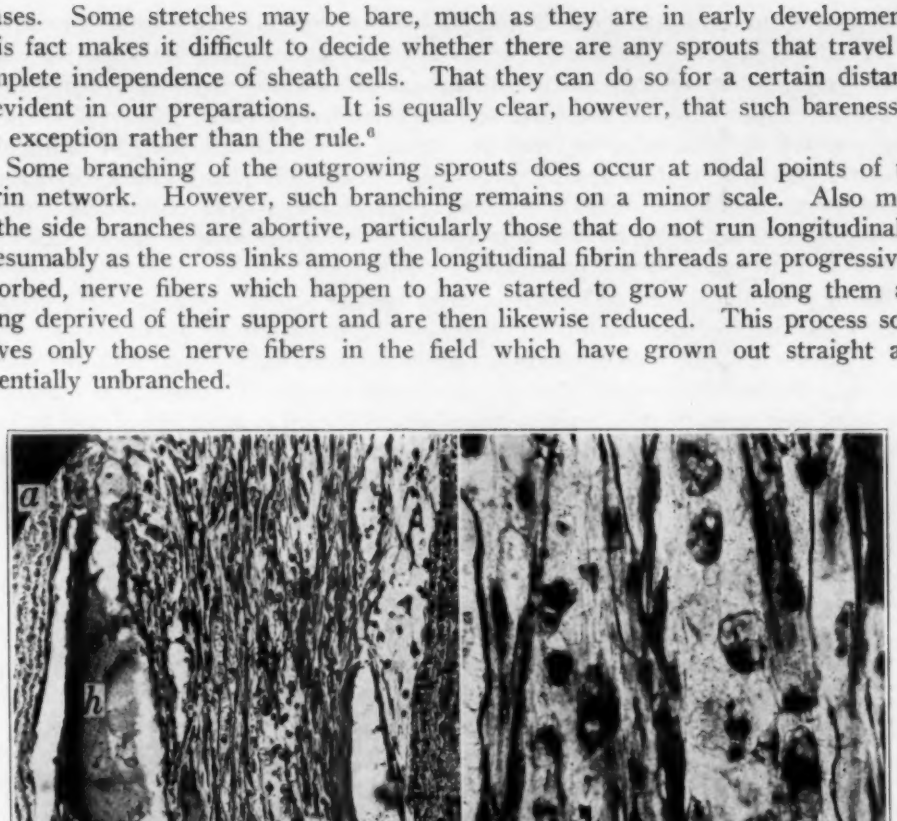

Fig. 7.—*A*, restored union between proximal and distal stump on the fifth day; *a*, sleeve wall; *h*, fresh hemorrhage (× 120). *B*, strands of sheath cells, axons and macrophages in the union tissue of the same case as shown in figure 7 *A* (× 630).

FIVE DAYS

By the fifth day, the orderliness of the reconnection between the proximal and the distal stumps has become fully apparent. By now, most of the union tissue has been pervaded by sheath cells and regenerating nerve sprouts, and the former clot has become fully converted into a new integral segment of nerve. As one can see from figure 7 *A*, the new nerve segment has cleanly retracted from the arterial wall, the space in between being taken up by a liquid residue of the pre-

5. Speidel, C. C.: (*a*) Studies of Living Nerves: I. The Movements of Individual Sheath Cells and Nerve Sprouts Correlated with the Process of Myelin-Sheath Formation in Amphibian Larvae, J. Exper. Zool. **61**:279-331, 1932; (*b*) II. Activities of Ameboid Growth Cones, Sheath Cells, and Myelin Segments, as Revealed by Prolonged Observation of Individual Nerve Fibers in Frog Tadpoles, Am. J. Anat. **52**:1-79, 1933.

6. Nageotte, J.: L'organisation de la matière dans ses rapports avec la vie, Paris, Félix Alcan, 1922. Kirk and Lewis.[2] Holmes and Young.[4]

ceding liquefaction. The streams of sheath cells, which have emigrated from the two nerve stumps, have met and merged into a continuous cell bridge. Restoration of their continuity obviously terminates their further migration and proliferation, for these sheath cell streams never show any tendency to continue to grow into local gliomas. Macrophages are now present in large numbers and by their liquefying power keep the channels between the outgrowing cell strands clear (fig. 7 *B*). Some scraps of the old fibrin network are still present in spots but are apparently being removed by the macrophages. At the same time, collagen begins to appear along the surface of the sheath cells, and the formation of neurilemmal sheaths and true endoneural connective tissue is thus initiated. Axons have continued to grow along the longitudinal pathways without further attempts at branching, and many of the most advanced sprouts have already penetrated into the distal stump, even in cases in which the original gap between the nerve ends measured as much as 5 mm. The original network of the clot has by now become completely resolved into a system of independent longitudinal strands.

SEVEN DAYS

By the end of the first week, the healing process is essentially accomplished. At this time, the former scar region can no longer be distinguished as such, and most traces of the former cut surfaces have become abolished, with the exception of the old margin of the perineurium, which has remained sharply outlined.[1] The nerve fibers extend now in strictly oriented straight and parallel strands from the proximal into the peripheral stump (fig. 8). They are still separated by larger liquid spaces than would be found in the normal nerve. These spaces, however, do not represent edema of the kind described in an earlier paper [7] but are residues of the local liquefaction which has been maintained throughout the healing process. Just when movement of endoneurial fluid along these spaces will be resumed, enabling such fluid to pass freely from the proximal to the distal stump, cannot be determined without special experiments. It is probable, however, that the endoneurial humors take over where the local liquefying activities of the healing process leave off in providing for fluidity of the nerve spaces.

LATER STAGES

A comparison of a splice after two weeks with that after one week reveals no new developments except an increase in the number of regenerated fibers. The new fibers tend to grow out along the surfaces of the more advanced ones, and thus small bundles are built up by a principle which has been described in an earlier paper [8] as "fasciculation." From then on, further improvement in the condition of the newly formed region will consist essentially of increase in the diameter of the nerve fibers, deposition of myelin and collagenization of the endoneurial tissue. Secondary resorption of excess collaterals, assumed to follow excessive branching and abortive sprouting in ordinary suture lines, is not encountered in our preparations, as branching has remained negligible.

As for the nerve sheath, the arterial sleeve may permanently serve as perineurium.[1] In many cases, however, enough epineurial tissue had been tucked into the sleeve during the operation to introduce a small source of epineurial proliferation into the lumen. However, since its growth is forced into the same longitudinal orientation that characterizes the rest of the union tissue, it merely forms a thin

7. Weiss, P.: Endoneurial Edema in Constricted Nerve, Anat. Rec. **86**:491-522, 1943.
8. Weiss, P.: Nerve Patterns: The Mechanics of Nerve Growth, Growth **5**:163-203, 1941.

Fig. 8.—Completed union on the eighth day; *a*, sleeve (× 48).

cylindric layer separating the nerve proper from the inner arterial wall. In no case have we seen an infiltration of this tissue into the interior of the nerve.

THE UNION OF ANEURITIC NERVE STUMPS

In the case of nerve grafts, the connection between the proximal nerve stump, as source of innervation, and the graft is effected in the manner described in the preceding pages. The union of the peripheral end of a graft with the distal nerve stump, however, is somewhat different, in that it involves the union of degenerated "aneuritic" nerve fibers, none of which contain axons. Since difficulties encountered by nerve fibers when they later reach the distal end of the graft have often been blamed for the lack of success of grafting in general,[9] we made a special investigation of the healing process at the "distal suture line." As was to be expected, the events there were in all essential points identical with those observed at the proximal suture line; i. e., the arterial sleeve had the same organizing effect on the union tissue and, in further consequence, on the reconnection of the two severed ends. There were some minor differences, however, attributable to the different constitution and consistency of the aneuritic fibers in this region.

As was outlined on page 420, the nerves of this series were allowed two weeks of predegeneration prior to the splicing operation. They were therefore in a different condition from nerves in primary suture. The nerve fibers had become converted into true Buengner cords; axons and myelin had disappeared, and sheath cell hypertrophy and hyperplasia had already led to the formation of relatively solid bands of protoplasm inside the neurilemmal tubes, in accordance with the classic descriptions by Ramon y Cajal, Boeke, Nageotte and others. In brief, the irritative and regressive changes following primary nerve section had subsided, and the cells were already in proliferation. Consequently, it was not surprising to find that the reconnection between such aneuritic nerve stumps after sleeve splicing occurred even more promptly than that between stumps after primary transection. While the general organization of the union tissue two days after the operation is much the same as previously described for that stage, sheath cell migration is already as extensive as it would ordinarily be about the fifth day. This difference is readily explained by the fact that after primary nerve section the sheath cells are not immediately in a condition to migrate and will not acquire this faculty until after the breakdown of the neurite, while in the predegenerated nerve they had already passed through this preparatory phase.[10]

Sheath cell growth occurs again along a foundation of oriented fibrin, which arises in the same manner as in primary sutures. Figure 9 shows the borderline between one nerve stump and the union tissue on the third day after splicing. It clearly illustrates how the fibrin network is connected with the old collagen system of the nerve. This favorable picture has been obtained because sheath cell emigration in this case had, for some unknown cause, been delayed. One recognizes the anchoring of the fibrin network all along the old surface of the nerve, the longitudinal fiber strands becoming heavy and straightened, while the transverse connections are being dissolved. A moderate number of leukocytes and a few macrophages can also be seen. The membrane-like border between the old nerve

9. Davis, L., and Cleveland, D. A.: Experimental Studies in Nerve Transplants, Ann. Surg. **99**:271, 1934.

10. Ingebrigtsen, R.: A Contribution to the Biology of Peripheral Nerves in Transplantation: II. Life of Peripheral Nerves of Mammals in Plasma, J. Exper. Med. **23**:251-264, 1916. Abercrombie, M., and Johnson, M. L.: The Outwandering of Cells in Tissue Cultures of Nerves Undergoing Wallerian Degeneration, J. Exper. Biol. **19**:266-283, 1942.

fibers and the fibrin lattice consists of collagen. It can be attributed to the fact that the cross section of aneuritic nerves contains a solid mass of cells and intercellular matrix, while the cross section of freshly transected nerves is riddled with the lumens of nerve fibers in initial degeneration. It is unlikely that this fine collagenous lamella could present a permanent barrier to nerve regeneration, since macrophages coming up against it from the old nerve tubes seem to puncture it promptly.

At the end of seven days, the continuity between the spliced nerve stumps is fully restored by cellular strands in straight parallel alinement. As seen in figure 10 *A*, the nerve again assumes the center of the sleeve lumen, while the space between nerve and wall is filled with residual liquid from the liquefaction of the

Fig. 9.—Transition from an aneuritic nerve stump (below) to the union tissue (above) on the third day (× 240).

clot. Blood vessels again pass straight from one stump to the other (fig. 10 *B*), following the general orientation of the union tissue. Figure 10 *B* gives a detailed view at higher magnification of the union tissue of the nerve shown in figure 10 *A*. One recognizes the long slender parallel cylindric bands of sheath cells, and a longitudinal blood vessel (*b*).

Preparations of this kind are particularly favorable for the study of the problem of collagen formation in nerves. This problem has aroused some interest in connection with the peripheral nerve tumors. Without entering into the neuropathologic aspect, we can state that our preparations make it absolutely clear that collagen is formed along the surface of the sheath cell. The longitudinal bands of sheath cells, being enclosed in a tubular neurilemmal sheath, are so characteristic in appearance that it would be impossible to confound them with the scattered elements of

the endoneurial connective tissue. In their outgrowth, the Schwann cell cords retain their characteristic tandem arrangement. While in an ordinary nerve scar these strands are intermingled with cellular elements of the scar region, the condition of the arterial splice lets them push forth into a cell-free medium, almost like tissue culture. We see these bands then glide along the fibrin strands into the former gap, often unaccompanied and undisturbed by any other types of cell. They represent, in a sense, pure cultures of sheath cells, and it is along their surface that the Mallory triple azan stain reveals the first identifiable deposit of collagen in distinct blue. Only later, finer collagen fibers appear in the spaces between individual cell bands, and even this may occur some time before endoneurial fibroblasts

Fig. 10.—*A*, completed union between two aneuritic stumps on the seventh day. *L*, levels of the old cut surfaces (× 76). *B*, detail of the union illustrated in figure 10 *A*; *b*, blood vessel (× 630).

have moved in. No similar collagen formations were ever observed around other sorts of cells in the early union tissue. These observations, therefore, fully confirm the view of Nageotte [11] and Masson [12] that collagen, and particularly the collagenous sheath of the individual nerve fiber, is a joint product of the sheath cell and its surrounding matrix, with the surface of the sheath cell as the seat of the primary action. The question of collagen formation in nerve is of considerable importance in connection with the practical problem of nerve fibrosis. It seems that serious

11. Nageotte, J.: Substance collagène et névroglie dans la cicatrisation des nerfs, Compt. rend. Soc. de biol. **79**:322-327, 1916.

12. Masson, P.: Experimental and Spontaneous Schwannomas (Peripheral Gliomas), Am. J. Path. **8**:367-416, 1932. Murray, M. R., and Stout, A. P.: Schwann Cell Versus Fibroblast as the Origin of the Specific Nerve Sheath Tumor, ibid. **16**:41-60, 1940.

attention should be given to the sheath cells in this respect, for they represent a potential intrinsic source of fibrosis.

NERVE REUNION WITHOUT SPLICING

As a background with which to contrast the effects of arterial splicing, we have made a number of control experiments in which a nerve was merely transected and the two ends then left in close apposition without further intervention. If the apposition was good, mechanical reunion between the ends took place within a surprisingly short time. After five days, the two ends were found to be firmly cemented by intervening scar tissue (fig. 11 *A*). However, the constitution of the union tissue was fundamentally different from that observed in sleeve-spliced nerves. The main points of distinction are the following: The liquefaction within the clot has failed to occur. Instead, dense fibrous connective tissue from the surfaces

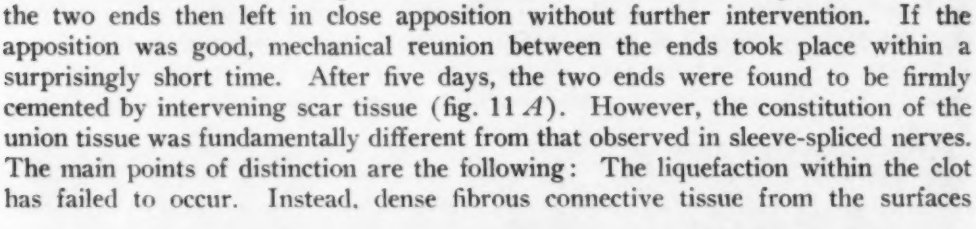

Fig. 11.—*A*, union between unspliced tibial nerve stumps on the fifth day. Note condensation and disorientation of scar tissue; *b*, epineurial blood vessels penetrating into the scar. The confused scar of this figure is to be compared with the well oriented union shown in figure 7 *A*, illustrating the sleeve-spliced peroneal nerve of the same animal; both nerves had been transected at the same level (× 63). *B*, enlarged view of the scar of figure 11 *A* (× 550). This figure is to be contrasted with figure 7 *B*, taken from the sleeve-spliced fellow nerve of the same animal.

of the nerve has penetrated into the region between the stumps and has given rise to a chaotic tangle of cells and fibers. Heavy lymphocytic infiltration accompanies the radial ingrowth of blood vessels from the vicinity. Adhesions between this scar tissue and its surroundings, resulting from the extraneural origin of these cells, cause the establishment of a tensional pattern which, in the main, converges radially toward the lesion. This is not conducive to the establishment of straight connections between the severed stumps. The outgrowing sheath cells and nerve fibers take correspondingly confused courses (fig. 11 *B*). As has been described by earlier observers, the regenerating axons branch profusely in the scar, with branches of the same fiber becoming distributed over widely separated regions of the scar and, hence, the distal nerve stump.

In short, unattended nerve stumps, even with cut surfaces closely approximated, fail to provide the conditions which we have recognized as indispensable for optimal nerve regeneration and which are actually obtainable by arterial splicing. The main shortcoming lies in the lack of lateral isolation of the union tissue. Indiscriminately adhering to the surrounding tissues as well as to the nerve ends, the initial clot develops a tensional pattern radiating in all directions and, consequently, preparing inroads from all sides for fibrous connective tissue. Moreover, as there are no provisions to prevent the dissipation of the proteolyzing factors from the union tissue, the latter cannot maintain that looseness of texture which ostensibly is a prerequisite of adequate nerve regeneration. As a result, instead of weaving an integral link between the nerve stumps, the union tissue becomes a foreign block in the continuity of the nerve. The fact that even so, owing to the luxuriant axon branching in such scars, numerous nerve fibers finally get through does not reduce the contrast between such unaided unions and the straight reunion of sleeve-spliced stumps. If we add that stitching the nerve ends with foreign suture threads, particularly in small nerves, only aggravates the disorganization of the tensional pattern at the suture line, the potential merits of sleeve splicing become apparent.

COMMENT

The observations reported in the preceding pages add up to a consistent and coherent picture of the healing process by which nerve stumps in an arterial sleeve are reunited. They likewise reveal the essential mechanisms involved. While individual cases show a certain variability of timing, the sequence of events is the same in all cases. These events duplicate essentially the course of action by which tension affects tissue growth in general and which was originally demonstrated and analyzed in tissue culture.[13] According to those earlier experiments, the mechanism operates in two phases: First, tension forces the colloidal matrix of the tissue to assume orientation along the lines of stress, which in turn gives rise to fibrillar arrangements of corresponding orientation; second, cells of the spindle cell type, when growing into the matrix, advance and proliferate along the oriented fibrillar framework of the matrix; as a result, the orientation of the cells coincides with that of the original tensions.[14] The same mechanism was later shown to underlie the oriented growth of nerve fibers as well.[15] At the same time, further evidence was obtained to show the active participation of the colloidal matrix in creating those tensions to which it owes its eventual organization. A matrix consisting of a fibrin clot, for instance, tends to shrink owing to the progressive segregation of the solid and the liquid phases (syneresis, coacervation). This sets up contractile forces in the solid parts. Tensions thus generated within the clot combine with those imposed from the outside. All this has been known from the tissue culture experiments. But we readily recognize now that exactly the same mechanism operates in the reunion of sleeve-spliced nerve stumps. It is supplemented, however, by some additional features which had not been previously recognized, as, for instance, the differential liquefaction of the clot. The primary role of the artery is to give this tensional mechanism free play. How it performs this role is briefly discussed in the following paragraphs.

13. Weiss, P.: Erzwingung elementarer Strukturverschiedenheiten am in vitro wachsenden Gewebe: Die Wirkung mechanischer Spannung auf Richtung und Intensität des Gewebewachstums und ihre Analyse, Arch. f. Entwcklngsmechn. d. Organ. **116**:438-554, 1929.

14. Weiss, P.: Functional Adaptation and the Role of Ground Substances in Development, Am. Naturalist **67**:322-340, 1933.

15. Weiss, P.: In Vitro Experiments on the Factors Determining the Course of the Outgrowing Nerve Fiber, J. Exper. Zool. **68**:393-448, 1934.

GAP FILLING

Nerve section invariably produces a gap between the stumps. Even what macroscopically appears as closest apposition still is a gap when viewed from the microscopic dimensions in which the cells that are to repair the defect operate. Gaps in tissue can be closed and repaired only by migration and growth of cells. This migration and growth can proceed only if certain physical and chemical requirements are satisfied, and foremost among these requirements is the presence of a proper physical substratum along which the cells may grow. Neither tissue cells nor nerve fibers can push forth into a homogeneous space, either gaseous or liquid; they extend only along phase boundaries (interfaces). The adequacy of a growth medium for cells and nerve fibers is, therefore, in part determined by its capacity to provide interfaces of the proper constitution, orientation, dimensions and numbers. The medium present between two severed nerve stumps is therefore of prime importance in that it must lay the foundation for the subsequent growth of a cell bridge.

Our experiments indicate that whole blood serves this function adequately. The fibrin of the blood clot furnishes the fabric subsequently to be molded by tensions into a system of tracks for cell and nerve fiber growth while the spacious meshes temporarily occupied by erythrocytes constitute spare room to be taken up by the invading cells. One must never lose sight of the fact that cells, like any physical bodies, can move into a circumscribed area only if they can displace a corresponding volume of substance. Liquids are easy to displace. However, if the clot consisted predominantly of compact matter, such as, for instance, fibrin, the cells would have much harder going and could penetrate only in limited numbers. It is for this reason that any filling above a certain density, even though having good cementing power and proper orientation, will be detrimental to nerve regeneration. This seems to be particularly true of pure or fortified blood plasma. Lacking the red cells, which after disintegration will contribute to the liquid phase, such a clot contains an unduly high ratio of solid fibrin to liquid constituents and therefore presents a handicap to growth. We have made a number of comparative studies, using blood plasma as filling in sleeves, and have found this medium almost invariably too dense for good nerve growth. It produces fibrotic islands leading to small local neuromas of arrested and choked nerve fibers. While the blocking effects of pure blood plasma may be negligible in the case of close apposition of the nerve ends, e. g., after "plasma suture,"[16] they would become definitely objectionable in the presence of a gap of even a few millimeters. We are still investigating the optimal composition of the gap filling, and if a matrix superior to whole blood should be found, the results will be reported at a later date.

Our observations have brought no confirmation of the earlier contention[17] that endoneurial fluid may be an important factor in determining the properties of the union tissue during the early stages of healing. While such fluid is probably instrumental in keeping the nerve channels clear after the first healing period is over, it seems to play no part in the establishment of the channels. Some contribution of the nerve ends to the gap filling is essential, however, in form of clotting factors. Whole blood enclosed in an arterial sleeve would remain liquid, owing to the anticoagulant properties of the wall of the sleeve. However, with nerve ends inserted, it clots.

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16. Young, J. Z., and Medawar, P. B.: Fibrin Suture of Peripheral Nerves, Lancet **2**: 126-128, 1940. Tarlov, I. M., and Benjamin, B.: Autologous Plasma Clot Suture of Nerves. Science **95**:258, 1942.

17. Weiss (footnotes 1 and 7).

TENSIONAL ORGANIZATION OF THE UNION TISSUE

The events of the second and third days are essentially concerned with transforming the original blood clot into a system of longitudinally oriented pathways for subsequent cell and fiber growth. This could be ascribed to some unknown "orienting factors" emanating from the two nerve ends, but both past experience and the evidence of the present experiments identify the operating factor as tension. These tensions arise partly outside, partly inside of the clot. Extraneous tension is due to whatever pull the nerve ends exert. There is a definite tendency of freshly cut nerves to retract beyond the initial distance during the days following transection. This gradual retraction works in the right direction, in that it places the union tissue under longitudinal strain. It is here that the elastic properties of the sleeve come into play. If the nerve ends are rigidly connected by sutures spanning the gap, all tensile stresses in the direction of the nerve will be taken up by the rigid suture threads, and the parts lying in between will sustain no stretch whatsoever. Only an elastic or plastic link permits the transmission of tensions to the substance filling the gap, where they may then exert their molding effects. As mentioned before, another effective source of tensions lies, however, in the shrinkage of the clot itself, and this type can of course operate even within rigid tubes or between nerve ends otherwise rigidly united, provided that the right amount of contractile material is present between the ends.

The configuration of the tensional pattern depends on how and where the clot is attached to its surroundings. No elastic tensions can develop in directions in which the material is free to contract. The points of attachment, therefore, determine the resultant stresses. An ideal pattern of longitudinally oriented stresses will arise in a clot attached at both ends to the nerve stumps but unattached over the rest of its circumference. The arterial sleeve is instrumental in bringing about this optimal tension pattern (fig. 12 *A*). It does so by preventing the clot from adhering along its sides. From its very beginning, the clot fails to bind intimately with the arterial wall. During the second and third days, this lack of adhesion is then further accentuated by active detachment from the sleeve. This is effected by migrating cells of the leukocyte type which spread rapidly along the wall of the artery and liquefy the adjoining surface layer of the clot (fig. 4). How many of these cells have emerged from the interior of the clot and how many have come from the nerve stumps, it has not been possible to determine. Some of them may be remnants of the arterial endothelium. However, most of the original lining is presumably scraped off during the splicing operation. Moreover, the lateral detachment has also been observed in sleeves made from frozen-dried arteries, in which the original endothelium had certainly perished. Whatever their origin, these cells produce a liquid layer which effectively separates the clot from contact with the sleeve. They might achieve this either by secreting a fluid or by secreting proteolytic enzymes which will digest the fibrin and thus liberate serum previously entrapped in the meshes of the coagulum. The presence of distinct erosion cavities around each cell (fig. 4) suggests proteolytic action.

Any residual local attachment between clot and arterial wall introduces distortion of the longitudinal tension pattern and entails a corresponding diversion of cell and fiber growth. The extreme of this condition is observed when severed nerve ends are left unsheathed (fig. 11 *A*). In these circumstances the clot is attached along its entire surface, which, moreover, owing to its continuity with the tissue spaces, is extremely irregular. Consequently, the pattern of tensions resulting from the gradual contraction of the clot is likewise irregular. Granting that blood seeps more readily into the extraneural spaces than into the rather tightly packed

nerve, it is obvious that the predominant orientation of the resulting fibrin framework will be in the direction of the tissue spaces, i. e., transversal with regard to the nerve. Radiating fibrous adhesions with ample pathways for the ingrowth of fibrous tissue and capillaries into the gap and outgrowth of nerve fibers and sheath cells from the gap would be the result. These hazards can be avoided only by preventing the clot from forming lasting lateral adhesions. It is in their effect on this early phase of the healing process that the various methods recommended in the past for wrapping or tubulating the suture line will have to be assessed. Their varying effectiveness in this regard may explain the great variability of results obtained by different authors. The arterial sleeve still appears to be the most natural preventive.

It is understandable now why even small breaks or pores in the arterial wall cause disturbances of nerve regeneration out of proportion to their actual size.

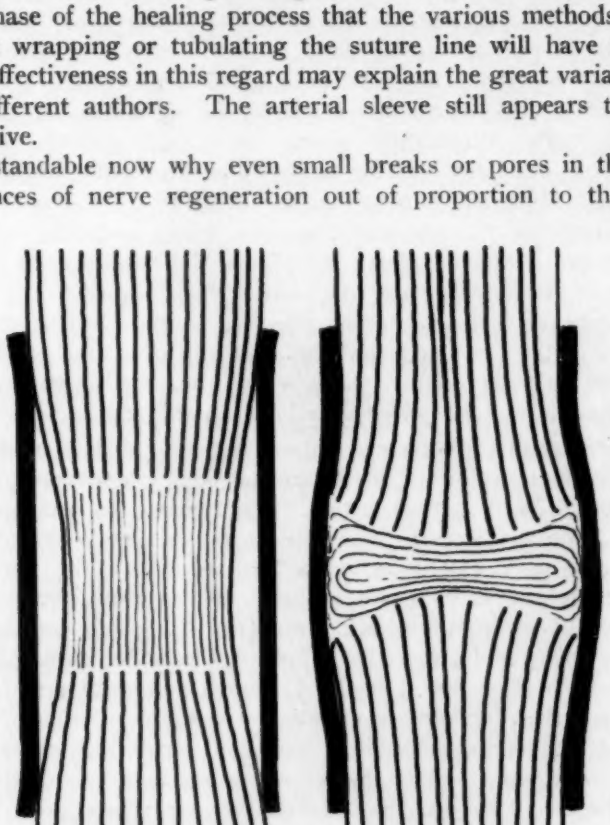

Fig. 12.—Diagram to illustrate the lines of stress in clots subjected to tension (*A*) or pressure (*B*) in the direction of the nerve.

They become centers of adhesion which deflect the whole tensional pattern in their direction (see fig. 5 of the earlier paper [1] on the subject). Similar difficulties have thus far militated against the use of heteroplastic arteries, both fresh and preserved. Large parts of the wall of a heteroplastic sleeve succumb to heavy lymphocytic attack in the foreign host body, and each focus of destruction becomes a potential source of adhesion and minor neuroma. If the host reaction could be delayed until there has been time enough for a well oriented union tissue to form, the sleeve would have served its main function, and the use of heteroplastic arteries might yet become feasible. On the other hand, there is no reason why other elastic tubes of nonirritant materials could not be substituted for artery, provided they

share the faculty of inducing fibrinolysis along their walls. Tubes fashioned from actively secreting epithelium or endothelium should serve this function adequately. We have found frozen-dried and rehydrated arteries fairly satisfactory, although occasional adhesions between union tissue and wall have been observed.

Aside from lateral adhesions, a major source of deflection of the tensional pattern is pressure of the two nerve ends against each other. Attempts at producing "close apposition" will have this effect. The nerve ends will become flanged and any blood clot forming in between, if it has no lateral outlet, will become subjected to compression in the direction of the nerve. The resulting tension pattern is shown in figure 12 *B*, and an actual example in a three day old splice is presented in figure 13. As subsequent growth of sheath cells and nerve fibers would retrace the fibrin pattern, the detrimental effects of this kind of union on nerve regeneration can easily be predicted from the pictures. By analogy we may assume that the presence between the nerve ends of air bubbles or liquid with excessive turgor will have similar effects.

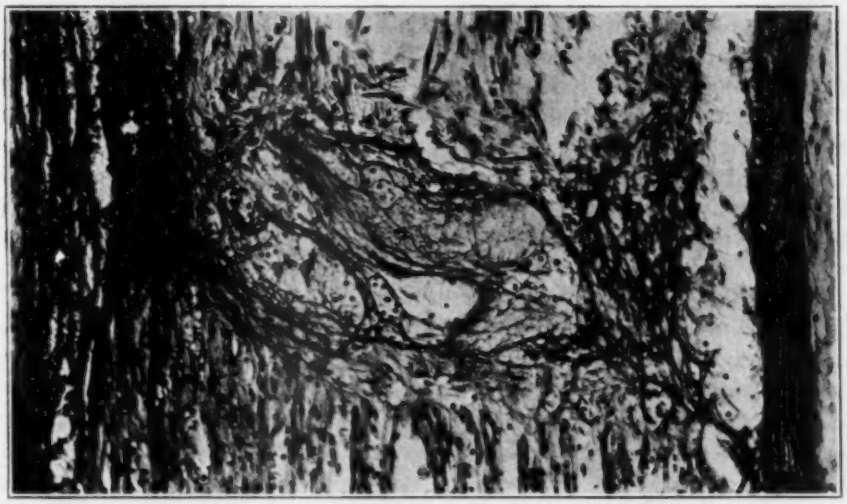

Fig. 13.—Transversally oriented union tissue between improperly set aneuritic stumps on the third day (× 120).

Once the correct tensional pattern has been established, the further course of events takes place almost automatically. The stress pattern first produces a corresponding orientation of the fibrin. The fact that oriented tension causes fibrin orientation in blood plasma clots has been a matter of record.[18] It is evident from our preparations that the fibrin fibers not only assume preferential lengthwise orientation but become heavier when oriented along the lines of stress. This increase may be ascribed to the greater ease with which smaller fibrillar units can aggregate into larger bundles when they are parallel. Eventually the lines of stress become thus embodied in a system of material lines of fibrin destined to form pathways for cells and fibers. This constructive process is soon joined by a destructive process in which the formation of oriented structures is further accentuated by the simultaneous destruction of unoriented ones.

18. Baitsell, G. A.: A Study of the Clotting of the Plasma of Frog's Blood and the Transformation of the Clot into a Fibrous Tissue, Am. J. Physiol. **44**:109-131, 1917. Nageotte.[6] Weiss.[13]

LIQUEFACTION

The dissolution of the interior of the clot begins about the second day (fig. 5 *A*) and from then on proceeds fairly rapidly. Biopsies after the second day usually show the sleeve filled with a pinkish fluid of low viscosity. This liquid menstruum is still rich in coagulable colloids, which when treated with the ordinary histologic fixatives produce a fine granulation. They give a strong Millon reaction for protein. Inasmuch as this liquefaction spares the heavier fibrin threads, which are oriented longitudinally, it does not lead to complete destruction of the clot but merely loosens its texture. In establishing longitudinal liquid channels, it prepares the ground for the later invasion by cells and fibers and, at the same time, counteracts any tendencies of the clot to become too compact and dense. In view of this fact, this phase of proteolysis seems almost an indispensable prerequisite for good nerve regeneration. The source of the liquefying agents becomes, therefore, a problem of considerable interest. While the problem has as yet been given only casual attention, the following facts have been gathered from our various observations.

Erythrocytes begin to disintegrate soon after the operation, and most of them have been destroyed by the second day. It is doubtful, however, that they release in their breakdown fibrinolytic enzymes, since it is unlikely that such enzymatic action would have remained undiscovered. A more familiar source of proteolysis is present in the blood clot in the form of granular leukocytes.[19] Studies on inflammation, as well as tissue culture observations, indicate that such white cells begin to disintegrate after about twenty-four hours, and, inasmuch as they are known to contain proteolytic enzymes, the liberation of such agents en masse at the end of the first day would readily explain the observed onset of liquefaction just about that time. A third possibility, namely, the exudation from the nerve itself of fluid rich in proteolytic enzymes,[7] cannot be wholly excluded, but our preparations reveal no fact that would encourage this view. If it were correct, liquefaction of the clot should proceed from the nerve ends toward the middle; yet no such systematic progress has been observed. On the contrary, centers of liquefaction are usually scattered more or less evenly throughout the clot (figs. 5 *B*, 6 *A* and 9). The fibrinolysis of the clot has no relation to blood vessels. It may appear prior to the ingrowth of blood vessels, or, in the case of early revascularization, it occurs wholly independently of the locations of the young vessels.

Proteolysis attacks first the fine tracery of fibrin outlining the spaces formerly occupied by the erythrocytes. Thus the meshes of the fibrin reticulum become larger and larger. It is only then that macrophages appear on the scene in larger numbers. A few scattered macrophages have been observed from the very first stages (figs. 5 *A* and 9). Wherever present, they liquefy the immediate surroundings. However, they are too scarce at first to be considered as the main agents of the primary liquefaction. After the third day, however, they become much more abundant, particularly in those parts of the clot adjoining the cut surfaces of the nerve (fig. 7 *B*), and from then on they seem to take a definite part in further fibrinolysis. Their accumulation around the nerve ends leaves no doubt that they have emigrated from the nerve stumps, for there is no other source that could have provided them. As they push toward the middle of the clot from both ends, they dissolve whatever fine interconnections between the longitudinal fibrin strands have survived the preceding stage of liquefaction. The

19. MacCallum, W. G.: A Text-Book of Pathology, ed. 6, Philadelphia, W. B. Saunders Company, 1936.

appearance of the macrophages, therefore, marks a secondary phase of intensified proteolysis. It is possible that this is followed by a tertiary phase during which the longitudinal channels are held open by endoneurial fluid seeping in the proximodistal direction. This point, however, requires further examination. It is noteworthy that when a long tube of artery is attached to the end of a proximal nerve stump, with the free end ligated, it is found to be filled with fluid on the second day. When drained, the fluid is reformed. It has been observed as late as nineteen days after the operation.

The most remarkable feature of the liquefaction processes is that they spare that part of the fibrin network which has been oriented longitudinally under the influence of tension. Evidently this longitudinal fiber system is somehow protected against the proteolytic erosion. How this protection is achieved is still unknown. Two possibilities come to mind. The protection may be only apparent, in that the persistence of these fibers might merely be a result of their much larger size. In this case, all fibers would be attacked by the fibrinolytic enzymes indiscriminately, but the heavier ones would last longer, and the period of about one week, during which they serve as climbing ropes for the pioneering cells and fibers, would be insufficient for their complete dissolution. The other possibility is that the tensional orientation may have forced the surface molecules of the longitudinal fibrils into a more orderly and closer packing, which would provide fewer loopholes for the entry of proteolytic enzymes into the bodies of the fibers.

By the combined effects of tension and fibrinolysis, the framework of the nerve stumps has been rewoven throughout the former gap. The connecting fibrin threads now serve as guides for the outgrowing sheath cells and axons.

CELL INVASION

Ever since the classic experiments of Harrison [20] in tissue culture, the tendencies of cells to glide along fibrous structures have been known. The precise mechanism by which cells, and nerve fibers as well, are made to glide along surfaces is not known, but present evidence indicates that interfacial tensions are operative.[8] Our observations merely reaffirm earlier experiences. With the utmost clarity, the pioneering sheath cells can be seen to move from the nerve stumps into the union tissue along the fibrin fibers which they encounter at the very exits of the old nerve tubes. As we have previously said, these fibrin fibers are firmly anchored at the orifices of the neurilemmal tubes, and the emigrating sheath cells can therefore glide on into the scar along uninterrupted rails. Sheath cells emerging from the opposite nerve end behave similarly. As a result, the union tissue becomes populated with longitudinal, parallel, unbranched strands of sheath cells, with macrophages and occasional endoneurial cells interspersed (figs. 6*B*, 7*B* and 10*B*). Lack of branching of these cell strands may be ascribed to the same general principle established for nerve fibers, namely, that branching does not occur unless there is an incentive for it. Straight and unobstructed pathways offer no such incentive, and thus the sheath cells pass on straight from one stump to the other.

Evidently, sheath cells moving out from either end cease to migrate and proliferate as soon as they have made contact with similar cells coming from the opposite end. Whether it takes protoplasmic fusion or whether mere surface contact is sufficient to stop further growth seems irrelevant in the present connection. The main fact remains that the presence of straight guide lines between the two stumps insures that practically all sheath cells will be led head on against other sheath

20. Harrison, R. G.: The Reaction of Embryonic Cells to Solid Structures, J. Exper. Zool. **17**:521, 1914.

cells, thereby terminating growth in that particular line. In the end there will be just straight, simple bands of sheath cells connecting the two stumps (fig. 10 *B*), and no trace of the extensive gliomas so commonly found around nerve stumps.[21] By the same token, the formation of neuromas by the regenerating axons of the proximal stump is averted. The very fact that the mechanism: tension → fibrin orientation → tissue growth, operates equally well in the presence or absence of neurites guarantees that sleeve-splicing between a graft and a peripheral nerve stump will leave no distal suture scar but will establish smooth and straight pathways for the later passage of nerve fibers from the graft into the periphery (fig. 10 *A*).

AXON REGENERATION

By the time the axons of the proximal stump have recovered from their ascending traumatic changes and are ready to grow out anew, the main guiding features of the union tissue have already been laid down and the outgrowing fibers find a straight and direct pathway to the peripheral stump all prepared. This pathway is still composed in part of the old fibrin matrix, but in part it consists already of strands of sheath cells. As was mentioned previously, the new axons grow preferentially along the sheath cell strands, although free advance has been observed sporadically.

There is no indication that nerve fibers and sheath cells are guided toward each other by specific attractions, and in fact there is much evidence against such a view.[15] On the other hand, it is quite evident that as soon as axon and sheath cell are in contact, they tend to stick together. To quote a remote analogy, there is no force of attraction between a dry thread and a wet thread, but once both have come together, they stick. It seems that this is all that is needed to explain the association between nerve fiber and sheath cell if we keep in mind that the regenerating axons have never actually lost contact with sheath cells, as both are enclosed in a common neurilemmal tube. Therefore, if a regenerating sprout were to proceed into the scar independently, it would first have to detach itself from the sheath cell processes to which it adheres. As this detachment is apparently difficult to achieve, most axons stay in contact with sheath cells. It is possible, moreover, that specific mutual contact affinities [8] between sheath cell and axon make this adhesion firmer than would be that between an axon and another type of cell.

The regenerating axons seem to glide with great ease along the surface of the sheath cell strands, for club-shaped enlargements of the axon tips, indicating damming of axonal substance before an obstruction, are very rarely seen in the union tissue of a successful sleeve-splice. The frequency of terminal axon swellings is in direct proportion to the obstructiveness of the scar, and their lack indicates unimpeded outgrowth. Pioneering fibers have been found advanced as far as 8 mm. from the level of regeneration on the eighth day. Allowing four days for the early reconstruction phase, this would indicate a growth rate of 2 mm. per day, including growth through the "scar."

Branching, which is as much a function of obstacles across the path of growth as is the formation of terminal bulbs, has likewise remained at a minimum. Whatever little there is occurs during the earliest phase of outgrowth, when the longitudinal fibrin strands still carry side connections. Axons sometimes bifurcate at the crotches, with one branch following the main stem, while the other turns off along

21. Dustin, A. P.: Les lésions posttraumatiques des nerfs: Contribution à l'histopathologie du système nerveux périphérique chez l'homme, Ambulance de "l'Océan" **1**:71-161, 1917. Nageotte.[6]

the side branch. The fact, however, that little evidence of such axon branching is seen after the fifth day, indicates that the progressive resorption of the transverse fibrin threads, robbing nerve twigs attached to them of their support, must also have entailed the resorption of those axon collaterals. Only the straight fiber stem would thus be left to survive, or perhaps the vigor with which the nerve fiber advances in the main longitudinal direction drains growth requirements from the less vigorously growing collaterals and thus causes their atrophy. At any rate, the lack of branching can be definitely attributed to the orderliness of the preneural pathways. In contrast, branching in unspliced nerve unions or after faulty sleeve splicing is very profuse in accordance with the general disorganization of the scar.

The new nerve fiber tips of the proximal stump reach the level of the original cut surface usually several days later in sleeve-spliced stumps than in unspliced ones. This difference is explained by the fact that in the sleeve-spliced stumps the whole stretch of nerve inserted into the artery undergoes some traumatic degeneration. If this distance measures more than a few millimeters, it exceeds the normal range of ascending degeneration. The practical implications of this phenomenon would appear to be advantageous. It is a common experience that the segment lost by ascending degeneration is quickly repaired, inasmuch as the outgrowing fibers move unimpeded each in its own old tube. Consequently, their arrival at the nerve end would lag by no more than several days. On the other hand, their later arrival allows the union tissue more time to become organized and also gives the sheath cells, which move out from the level of section, a head start which they otherwise would not have. In fact, the more extensive ascending degeneration of the proximal stump may lead to the mobilization of a larger number of sheath cells than would normally be available at this end. It seems definitely more desirable to have the axons reach the gap only after the bed for their further growth has been properly prepared than to have them precipitated into the tangle of an early scar, which would leave marks of confusion in the restored nerve.

Our observations fully reaffirm the principle of contact guidance of the growing nerve fiber.[8] This principle states that the course of a nerve fiber is determined by the biophysical and biochemical organization of the surfaces along which the fiber moves, which implies that nerve fibers can move in no other way than by application to interfaces. On the negative side, the principle denies that agents not in immediate contact with the nerve fiber can affect its course, except indirectly by modifying the contact substrata. There is no "attraction" of nerve fibers toward distant sources of chemical emanations, such as are postulated in the theory of neurotropism.[22]

In spite of early opposition,[23] the theory of neurotropism has strongly influenced neurologic and surgical thought regarding nerve regeneration and nerve repair. The claim that degenerating peripheral nerve exerts a potent "attraction" on growing axons has been singularly intriguing. In view of the fact that surgical procedures based on this fallacious view are apt to be equally fallacious, it must be emphasized over and over again that this theory cannot stand up in the light of a critical evaluation of facts. To avoid repetition, we simply refer to previous

22. (*a*) Ramón y Cajal, S.: La rétine des vertébrés, Cellule **9**:119, 1893. (*b*) Forssman, J.: Zur Kenntnis des Neurotropismus, Beitr. z. path. Anat. u. z. allg. Path. **27**:407, 1900. (*c*) Tello, F.: Gegenwärtige Anschauungen über den Neurotropismus, Vortr. u. Aufs. ü. Entwcklngsmech. d. Organ., 1923, no. 33.

23. Dustin, A. P.: Le rôle des tropismes et de l'odogénèse dans la régénération du système nerveux, Arch. de biol. **25**:269, 1910. Ingebrigtsen, R.: Experimentelle Untersuchungen über freie Transplantation peripherer Nerven, Zentralbl. f. Chir. **43**:864, 1916.

presentations of the evidence by Weiss [24] and corroborative reviews by Harrison,[25] Detwiler [26] and Young.[27] The observations of Ramón y Cajal [22a] and Forssman [22b] that continuity is restored between severed nerve stumps even when the latter have been separated and brought out of line, are, of course, quite correct. However, this connection is effected not by "attraction" but by the influence of the stumps and their surroundings on the configuration of the union tissue, plus the fact that the earlier fibers making successful connections constitute a pathway of preferential application for fibers growing out later ("fasciculation").[8]

As a sample of additional evidence contradicting chemotropism in nerve growth, which will be reported more fully elsewhere, we cite the following experiment. A proximal nerve stump was inserted into the stem of a Y-shaped artery, with the fork offering alternative pathways to the regenerating fibers. A peripheral nerve stump was inserted into one of the open ends, while the other end was either left open or tied off or plugged with a piece of tendon. In no case were the regenerating nerve fibers "attracted" toward the peripheral nerve fragment, but the fiber stream divided itself more or less evenly and continued into both channels regardless of the kind of destination awaiting them.

Comparable observations were made in experiments mentioned previously, in which a proximal nerve stump was introduced into the end of a long arterial tube, the other end of which was ligated. This blind tube remained dilated first by blood, and subsequently by a liquid, composed presumably partly of fibrinolysate and partly of nerve exudate. There was a fibrin framework in the interior, much as in gaps between two nerve ends, and sheath cells and nerve fibers had grown in large numbers down the full length of the tube, only to be finally stopped at the blind end. They obviously grew toward no "destination," but simply along an established pathway with no exit. Growth in such arterial tubes is never as strictly oriented as it commonly is in sleeves between two stumps. Nevertheless, the main orientation is longitudinal. This may be attributed to the fact that adhesions of the ligated end of the arterial tube set the latter under longitudinal tension. Encouraged by these experiences, we are at present exploring the possibility of using stretched blood-filled sleeves in the role of grafts to bridge larger nerve gaps. This method would circumvent many of the shortcomings of the "tubulation" practices of the past.

FIBROSIS

Collagen formation in the union tissue sets in immediately after cell invasion. The role of the Schwann cell in this process has already been discussed. The earliest deposition of collagen in the otherwise fibrinous matrix appears along the surface of the Schwann cords. From there the process spreads into the interstices, establishing a new endoneurium. If it went no farther, collagenization would simply restore to the new nerve parts normal histologic features. However, in many instances it goes beyond limits compatible with the requirements of good nerve regeneration and nerve function. The result may be anything from moderate to serious fibrosis. The heavier the fibrosis, the denser the interstitial tissue will be; and the denser the tissue, the fewer nerve fibers will penetrate, the more will

24. Weiss (footnotes 8 and 15).

25. Harrison, R. G.: The Croonian Lecture on the Origin and Development of the Nervous System Studied by the Methods of Experimental Embryology, Proc. Roy. Soc., London, s.B **118**:155-196, 1935.

26. Detwiler, S. R.: Neuroembryology, New York, The Macmillan Company, 1936.

27. Young, J. Z.: The Functional Repair of Nervous Tissue, Physiol. Rev. **22**:318-374, 1942.

be prematurely arrested, the slower will be the advance of the successful ones, the less their ability to recover normal diameter and the greater their danger of becoming strangled and pressure blocked.

The arterial sleeve reduces the sources of fibrosis, but it does not altogether abolish them. It reduces fibrosis, first by shielding the interior from highly collagenous extraneural scar tissue, and second by turning whatever trace of fibroblastic tissue may have penetrated into the sleeve immediately into a longitudinal course parallel to the nerve, where it can do no harm. Naturally, these two protective features are predicated, the former on a hermetic seal between artery and nerve, and the latter on the presence of longitudinal stress. Accordingly, methods aimed at preventing fibrosis by tubulating or otherwise wrapping a nerve suture are apt to remain ineffective to the extent to which they fail to realize those two prerequisites. Yet, even with all extraneous sources of fibrosis excluded, there still remains the problem of intrinsic fibrous transformation, particularly of degenerated nerve. We have planned a special study of this problem and hope to be able to present tangible data at some later date. In the meantime, a few occasional observations deserve to be noted.

In a number of our cases, excess collagen was found in that portion of the distal nerve stump tucked into the arterial sleeve. The indications are that this represents a tissue reaction of the nerve to its compression by the sleeve. Compression is caused by the swelling of the peripheral stump during early degeneration (see figs. 1 and 2, Weiss,[7] 1943), which amounts to tightening of the arterial grip. In response, the nerve produces new collagen. When limited to a short segment, this may be innocuous. However, it seems that some such hypertrophy of collagen may occur throughout the distal stump, possibly as a direct reaction of sheath cells and endoneurium to the increasing turgor of the degenerating fibers. The excellent nerve fiber growth commonly observed in peripheral stumps indicates that hypercollagenization of moderate degree is no bar to successful regeneration. Evidently, later shrinkage of the degenerated fibers, with or without reinnervation, removes the internal pressure, which if it were kept up might easily lead to progressive fibrosis. Extraordinary circumstances, however, may lead to just that, and it is worth investigating whether some instances of intraneural fibrosis may not be blamed on irregularities of the degeneration process, such as, for instance, delay in the resorption of the "ovoids," congestion of the tubes with hyperplastic sheath cells, etc. Continued research into the causes of fibrosis, it is hoped, will produce measures of nerve repair which are not only "afibrotic"—keeping fibrosis out—but also "antifibrotic"—counteracting it where it has occurred. Preserving a certain fluidity of the nerve spaces seems to be a prime factor of success. The role of the endoneurial fluid in maintaining this fluidity has been suggested [7] but remains to be demonstrated.

Nerve grafts seem to be particularly susceptible to fibrosis, but without a detailed analysis it is impossible to give the reason for this change or to formulate possible means of averting it. Fibrosis of the densest sort is what makes alcohol-fixed nerve grafts unfit for use. While some nerve fibers may penetrate,[28] regeneration through the graft and its replacement tissue remains insignificant,[29] even though

28. Huber, G. C.: Operative Treatment of Peripheral Nerves After Severance, More Particularly After Loss of Substance: A Critical Review, J. Lab. & Clin. Med. **2**:837-848, 1916-1917. Nageotte.[6]

29. Sanders, F. K., and Young, J. Z.: The Degeneration and Reinnervation of Grafted Nerves, J. Anat. **76**:143-166, 1942.

the orientation of the tissue is of the required kind. We have convinced ourselves of this fact in experiments on the rat.

In conclusion, it can be stated that proper orientation of the matrix is not enough to insure optimal nerve regeneration; the matrix must also be of the right composition, and this includes a correct balance between collagenous and noncollagenous constituents.

CONCLUSIONS

In the light of our analysis, the arterial sleeve appears to fulfil a variety of functions.

1. It unites the nerve ends. However, the initial holding power of this link is not sufficient to withstand more than moderate tension. It could not maintain a forcible approximation of the nerve ends such as may be attempted for the reduction of a sizable nerve gap. In such cases, stay sutures at a safe distance from the nerve ends could be used to take up the main stress, leaving just enough stretch to keep the union taut. The presence of some blood-filled gap between the cut surfaces seems imperative.

2. The sleeve serves as container for the cementing blood clot.

3. By liquefaction along its inner walls, it prevents lateral adhesion of the union tissue. This throws all tensional stresses into a strictly longitudinal direction, thus bringing the fibrin matrix of the union tissue into alinement with the severed nerve fibers and creating a guiding pattern for the transit of cells and axons across the former gap.

4. The sleeve prevents the dissipation of the products of liquefaction, as well as of endoneurial fluid, and thus preserves a degree of fluidity optimal for nerve regeneration.

5. The sleeve prevents the ingrowth of extraneural connective tissue into the gap, as well as the escape of sheath cells and axons from the nerve. This it achieves not so much by grossly walling off the interior from the exterior, as by permitting a tissue matrix to form which will deflect all cell and fiber streams in the longitudinal direction.

6. This action likewise accounts for the lack of branching among the outgrowing axons and Schwann cords and for the suppression of the neuromas and gliomas which would otherwise develop.

7. The sleeve permits direct vascular reconnection between proximal and distal stumps through the gap, while excluding the intrusion of extraneural blood vessels. Whether there is any significance to this point remains to be determined.

These points constitute the crucial advantages of arterial sleeves. The list can serve a double purpose. Firstly, if the use of arteries should prove impracticable in man one could try to resort to composite procedures, i. e., substitute for the single action of the arterial sleeve a combination of measures, for instance, one providing for the sealing, another for the tension pattern, a third for liquefaction, etc. Secondly, the list establishes criteria by which the prospects of tubulation and wrapping procedures in nerve repair may be assessed. Unless such procedures score favorably when tested point for point down the list, they are not likely to measure up to the results hitherto obtained with arterial sleeve splicing. A survey of the literature on tubulation shows that many past procedures falling in that class bear only superficial resemblance to arterial sleeve splicing. None of them fulfils vigorously all requirements of our list. Some are excellent in one respect but fail in others. Practically all of them deprive the union tissue of the benefit of longitudinal tension. Others leave spaces between tube and nerve, perhaps small

in macroscopic terms but huge for cells which operate in microscopic dimensions. Still others introduce foreign substances, such as gelatin or agar-agar or air, into the gap, creating a situation diametrically opposed to what would aid the nerve. The idea that a medium will be favorable for nerve growth just because it is "soft" or "nutrient" or rich in vitamin B_1, etc., is based on a serious misconception of the mechanism of nerve growth. Such notions can usually be traced to the tempting analogy between a nerve sprout and a plant root. Yet nerve fibers decidedly do not grow after the fashion of plant roots. They grow by surface application, and the physical configuration of their matrix is as important as is the chemical composition of the medium.

To replace conjectures about the requisites of nerve regeneration by factual knowledge seems the only safe way toward the creation of a solid and rational basis for the improvement of nerve repair. The present article is presented as a contribution toward that goal.

SUMMARY

A study of the processes following the reunion of severed nerve ends by an arterial sleeve in the rat has revealed a typical sequence of events, as follows:

A blood clot cements the nerve ends.

Within a day the red cells break up, leaving the fibrin net of the plasma standing.

Owing to liquefaction along the arterial wall, the union clot becomes detached laterally, while remaining firmly fused to the nerve ends.

This results in longitudinal tensions transmitted from nerve to clot to nerve.

These tensions orient the fibrin fibers in longitudinal directions.

Proteolysis throughout the clot, beginning about the second day, gradually destroys all fibrin fibers except the ones oriented lengthwise. Thus a system of longitudinal fibrin strands bridging the gap from stump to stump is established.

Macrophages move into the gap, continuing the clearing of liquid channels. Sheath cells move out from both nerve stumps, glide along the fibrin rails and give rise to the deposition of endoneurial collagen on their surfaces.

Axons regenerate, mostly in application to sheath cells, along the same straight and direct guide lines. Lacking obstructions, they proceed essentially without branching.

The main framework of the nerve union is completed by the end of the first week, and subsequent developments concern mainly the utilization of the bridge by increasing numbers of nerve fibers and the maturation of the latter.

These experiments have established a number of conditions prerequisite for optimal nerve regeneration. They point the way toward the avoidance of confused suture lines, neuromas, gliomas and nerve fibrosis. Even if the arterial splice as such should not be applicable in clinical practice, the lessons learned from this analysis of its merits may guide the search for improved methods of nerve repair.

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EVALUATION AND TREATMENT OF FACTORS INVOLVED IN POSTLOBECTOMY COLLAPSE OF THE LUNG

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The initial stage in the surgery of pulmonary resection has now passed. In the pulmonary as in every region of the body when emerging within the scope of surgical intervention, operation carried with it a high mortality rate. But in the last decade the rate associated with lobectomy has steadily declined from 50 per cent to an average of 10 per cent, and it is even as low as 2.5 per cent in certain clinics for patients with diseases of the chest. Now the emphasis has shifted from the immediate risk of resection of a progressive and eventually fatal lesion to the securing of the maximum postoperative function for the patient. Actually today both these problems are one, namely, the prevention of postoperative collapse of the lung.

CAUSATION OF POSTLOBECTOMY COLLAPSE OF THE LUNG

Collapse of the lung after lobectomy is of two distinct types, depending on whether the involved lobe shows complete or incomplete airlessness.

The complete form, or apneumatosis, is caused by conditions which prevent the circulation of air while maintaining the circulation of the blood in any area of the lung. The collapse is due to the elastic recoil of the lung as the entrapped air is absorbed into the blood stream, while the loss of further aeration may be produced either by complete bronchial obstruction from an intraluminal block or by bronchiolar obstruction due to pressure from without, such as a pleural effusion which abolishes both the intrapleural subatmospheric pressure and the cohesion of the visceral to the parietal pleura.

In the second, and more common, form there is lack of expansion of the remaining lung tissue to fill the thoracic cavity, though occasionally this is due to inadequate compensatory distention. This form of collapse may be produced by fibrosis following inflammation of the lungs and the pleura. But to be of much consequence the process must be diffuse, for a local lesion is readily compensated for by increased distention of the healthy lung tissue. Other factors also are credited with the production of this form of collapse. For instance, alteration in the vascular supply to the lung has a definite effect. Ligation of the pulmonary artery is followed by shrinkage and collapse, with fibrosis of the corresponding part of the lung. Ligature of the bronchial arteries produces no effect, but if it is combined with ligation of the corresponding pulmonary artery, gangrene ensues. Ligation of the pulmonary veins is followed by stasis and engorgement; these may be lethal, though the collateral return usually suffices. It has been repeatedly stated that there is a reflex form of collapse, but there does not appear to be any conclusive evidence of it. That such collapse is not due to paralysis of the muscles of respiration is shown by the numerous patients with phrenic evulsion and intercostal neurectomy who do not have collapse of the lung. It has been suggested

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that reflex collapse is produced either by bronchial spasm or by angioneurotic edema, but clinically and experimentally both these conditions are found to lead to emphysema and never to collapse, as complete obstruction does not occur from these factors alone. Factors of unknown importance in the collapse of a lung are those of interpleural surface tension and cohesion. Apparently they account for the fact that the lungs do not collapse when the intratracheal pressure is made considerably less than the intrapleural pressure, but their precise role is so far undetermined.

At present the known factors in the production of postlobectomy collapse are bronchial obstruction and fibrosis, and the latter may be caused either by infection of the remaining lobes or by operative trauma to their arterial supply through the pulmonary arteries. Clinically, collapse after lobectomy appears to be of three main types (Churchill [1]). The first type is due to the pressure of an encysted collection of fluid, which is usually apical in position. The second type is massive collapse. This is due to bronchial obstruction, and the affected lobe is almost invariably found to be adherent to the wall of the chest. And the last type, which I think is the most common and certainly is the most dangerous, is due to chronic progressive infection of the lobe with subsequent diffuse fibrosis. The fibrosis probably starts around areas of destruction of tissue in the bronchioles. However, it may be due to growth of granulation tissue into a long-standing alveolar exudate, the stasis being due either to inadequate vascular and lymphatic absorption or to deficient bronchial drainage.

The infection must be diffuse. I had a patient in whom the lower lobe of the left lung was resected for bronchiectasis and six weeks later an abscess developed in the nearly expanded upper lobe with resultant complete collapse. After drainage of the abscess expansion took place and only a small thoracoplasty was needed to complete the cure. At the time of writing he has remained well for over a year, can walk 10 miles (16 kilometers) without fatigue and has negligible cough and sputum.

It is especially to prevent chronic progressive infection that meticulous care must be taken in the handling of the patient. In fact, evaluation and the treatment of factors involved in postlobectomy collapse require a survey of all the possible causes of bronchial obstruction and of pulmonary infection and fibrosis together with their treatment in the preoperative, the operative and the postoperative management of a patient.

PREOPERATIVE STAGE

Before operation an estimate of the degree of fibrosis already present in the lung and hence of the postoperative chance of incomplete expansion and the need for thoracoplasty can be made from the history and the roentgen examination. The majority of patients suitable for lobectomy have recurrent attacks of pneumonia, and it is my impression that if these attacks are limited to the proposed area for resection the prognosis is far better than if other lobes are involved as well. A more reliable estimate can be made during bronchographic examination, when the degree of movement at the interlobar regions can be observed. If movement is markedly diminished, it is almost certain that fibrosis has spread through the interlobar septum and involved the apparently unaffected lobe, with consequent increased risk of its postoperative collapse. I find this is better observed by screening than

1. Churchill, E. D.: Personal communication to the author, 1941.

by the study of bronchograms taken in different phases of respiration, and I consider it of more prognostic significance than the degree of atelectasis of the diseased lobe. In fact, I have been unable to find any definite relation between the degree of preoperative atelectasis of the diseased lobe and the postoperative expansion of the remaining lung tissue, though such a relation is frequently assumed to exist.

In the routine methods employed for the diagnosis of pulmonary lesions there appears to be an element of risk. The insufflation of powder does not give satisfactory definition unless the bronchial tree is practically dry; in view of this, iodized oil has been introduced. Iodized oil gives excellent bronchograms, but from time to time there have been reports of pneumonia following its use, and it

Fig. 1.—Bronchogram taken nine days before death showing that the lower lobe of the left lung has been removed and that the animal is not suffering from a drowned lung.

has been suggested that it is a cause of postlobectomy collapse (Belsey [2]; Gowar and Gilmour [3]).

To obtain controlled evidence of its effect, 25 cats were used. Rabbits were not employed because their physiologic makeup is so different from that of man; for instance, they cannot cough. The cats were anesthetized with appropriate intraperitoneal doses of pentobarbital sodium; an intratracheal catheter was passed, and amounts up to 5 cc. of iodized oil (3 different preparations were used) were injected. Small amounts of cocaine were sometimes injected before the iodized oil, but this made no difference in the results. Roentgenograms were taken to show the accuracy of the injection, and the animals were examined postmortem from one day to thirty-two weeks afterward. Some of the animals were subjected to

2. Belsey, R. H.: Brompton Hosp. Rep. **6**:133, 1937.
3. Gowar, F. J. S., and Gilmour, J. R.: Brit. J. Exper. Path. **22**:262, 1941.

lobectomy in the interim. Three had a second injection by the same method; 2 were given the second injection six weeks after the first, and in the case of the third eleven weeks elapsed between the injections. One cat had three injections; the two later injections were given two and eight weeks after the first introduction of iodized oil.

Lipid pneumonia occurred in 3 of the cats.[3a] The first had had one injection of iodized oil and died of anoxia four weeks later, immediately after lobectomy. One lobe showed small areas of lipid pneumonia. The second cat had the first injection four weeks before excision of the lower lobe of the left lung and the second injection two weeks after the operation. Five days later the animal was cyanosed and not eating. On the ninth day after injection, being moribund, it was killed with chloro-

Fig. 2.—Photograph of the right lung showing the typical pale yellow areas of lipid pneumonia.

form, and large areas of collapse due to lipid pneumonia were found in all the remaining lobes. The third cat also had the first injection four weeks before excision of the lower lobe of the left lung and the second injection two weeks after operation. It died of diffuse lipid pneumonia two weeks later.

No relation was observed between the length of time iodized oil remained in the lungs and the onset of lipid pneumonia; roentgenograms showed large quantities in some animals for as long as a month without any untoward effect. No other histologic change was found that could be attributed to iodized oil. Whether such a condition plays any part in postlobectomy collapse in man is doubtful. With Mr. J. E. H. Roberts' permission I have been able to examine the notes and roentgenograms of 50 of his cases at the Brompton Hospital, London, England.

3a. Chesterman, J. T.: J. Path. & Bact. **54**:385, 1942.

I can find no relation between the dates of administration, the number of administrations, the quantity of iodized oil used, the amount of iodized oil still present in the lungs at the time of operation as shown by roentgenograms and the extent of postoperative collapse of the remaining lobes. In this connection it is worth noting that postoperative collapse on the side not operated on is rare, occurring in only 2 of 51 cases of collapsed lobe in Tudor Edwards' series cited by Gowar,[4] though bronchograms had been made of both lungs.

In order to minimize the risk of postoperative infection it is essential that retention of secretions in the respiratory passages be avoided. Nasal sinusitis should be treated by adequate drainage, but radical procedures should not be resorted to until after the extirpation of the pulmonary lesion, for the continual coughing of purulent sputum makes the eradication of nasal sepsis impossible.

For drainage of the bronchi the most common method is postural drainage, but this to be effective must be practically continuous, since any relaxation of position allows repooling to take place. Its main value is for children, whose cough

Fig. 3.—Roentgenogram of the right lung showing iodized oil present in the areas of lipid pneumonia.

is often ineffectual and who can be maintained in the correct position for twenty-three hours a day. In the treatment of adults it is useful for short periods after an exacerbation of infection, but bronchoscopic aspiration, repeated if necessary, is far more effective, for it breaks up and removes the viscid secretion which collects in the dilated bronchi, and it stimulates coughing by its mechanical irritation.

The most satisfactory routine method appears to be the use of the creosote chamber, which increases expectoration by the physiologic method of stimulating the cough reflex. I have subjected mice to concentrations of vaporized creosote B. P. six times stronger than that used for human beings for four hours a day and six days a week and found no ill effect discernible either by the naked eye or on microscopic examination of a section of the lungs taken at necropsy up to fourteen weeks from the onset of treatment.

The method adopted should be continued until there is no further decrease in the amount of sputum voided and for at least a month after the last attack of infection of the respiratory tract has subsided.

4. Gowar, F. J. S.: Brit. J. Surg. **29**:3, 1941.

My impression is that patients with an efficient cough reflex as shown by the rapid expectoration of iodized oil are less liable to suffer from postoperative infection than others whose processes of elimination are less satisfactory.

The preoperative attempt to prevent collapse by the formation of adhesions between the visceral and the parietal pleura has attracted considerable attention, for if fusion of the pleura in given areas could be produced safely, it would prevent both any movement of the mediastinum during the operation and the complete collapse of the remaining lung tissue afterward.

Many methods and agents have been used to induce this condition (Bethune [5]; Singer [6]; Hanrahan, Adams and Klopstock [7]; Gowar and Gilmour [8]). I have tried silver nitrate, zinc sulfate, iodized talc and benzomastic. The last-named compound produces no apparent reaction, and of the two others silver nitrate produces in both cats and rats marked pleural effusions (unless used in a concentration sufficient

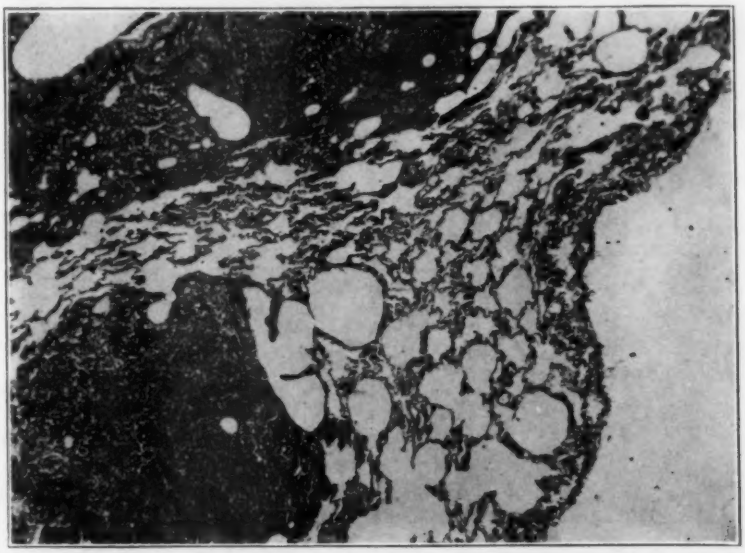

Fig. 4.—Low power photomicrograph of an area of lipid pneumonia, also showing normal lung tissue and pleura.

to damage the parenchyma of the lung) when adhesions are formed, but necrosis and death also may occur. Zinc sulfate, too, is variable in the reaction it causes.

Talc powder containing 0.5 per cent iodine has been found the most reliable agent by the majority of workers, and the results of its use have been studied in 22 cats. These were anesthetized by intraperitoneal administration of pentobarbital sodium, and in 17 poudrage was performed, either by blind insufflation through a small intercostal incision or under direct vision with a larger incision, the object being to fix the upper lobe. The method did not appear to affect the result, for all 5 cats killed in the first three days after poudrage showed a uniform diffuse distribution of the powder in the pleural cavity. After a week the powder was

5. Bethune, N.: J. Thoracic Surg. **4**:251, 1935.
6. Singer, J. J.; Jones, J. C., and Tragerman, L. J.: J. Thoracic Surg. **10**:251, 1941.
7. Hanrahan, E. M.; Adams, R., and Klopstock, R.: J. Thoracic Surg. **10**:284, 1941.
8. Beecher, H. K.: Acta med. Scandinav., 1938, supp. 90, p. 146; J. Thoracic Surg. **10**: 202, 1940.

mainly found on the mediastinal surface aggregated into small collections. Adhesions may commence to form on this aspect as early as the fifth day.

Excision of the lower lobe was performed on 7 animals on the fourteenth day. Three showed firm adhesions round the upper lobe, while the lower lobe was practically free; 2 showed marked mediastinal adhesions of both lobes; 1 showed marked basal adhesions only, and 1 showed both basal and apical adhesions. Thoracotomy performed on or after the twenty-first day showed firm adhesions of part or of the whole of the lung to the surrounding structures in every case. This confirms previous observations that iodized talc produces adhesions but that the position and the extent of these cannot be controlled. In estimating the result of this aseptic pleuritis it is necessary to consider the effect of the iodized talc on the pleura and the subjacent lung and also the effect of the adhesions thus produced on the postoperative expansion of the remaining lobes.

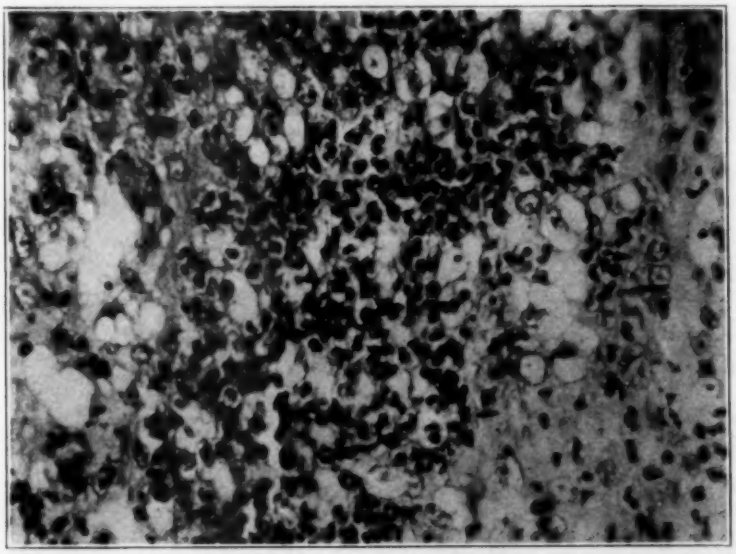

Fig. 5.—High power photomicrograph of an area of lipid pneumonia showing phagocytic cells containing large globules of lipoid, proliferation of cells in alveoli and a polymorphonuclear response.

As far as could be judged there was no toxic effect after insufflation of the powder, which at the end of a week tended to agglomerate and give rise to focal reactions with fibroblastic proliferation, a macrophage response and occasional giant cells. The subjacent lung did not appear to be in any way affected, nor could crystals be seen in the pleural and superficial pulmonary lymphatics. No involvement of lymph glands was seen.

The effect of these adhesions on the lung have been studied both before and after lobectomy. Of 9 cats examined before operation, between two and six weeks from the date of poudrage, 1 showed 50 per cent collapse of the upper lobe, which was bound down by the artificially produced adhesions. In the postoperative series 2 animals examined (one eight weeks and the other sixteen weeks after operation) were found to have the remaining lobe of the same size as before operation, adhesions having prevented compensatory distention. One animal, examined ten weeks after lobectomy, showed irregular expansion of the upper lobe with areas of emphysema and areas of collapse due to contraction of the adhesions.

A fourth animal, fifteen weeks after operation, showed diffuse fibrosis of the remaining lobe, which was firmly adherent to the apex of the thoracic cavity, and a fifth animal, eight weeks after operation, showed practically complete collapse of the remaining lobe. This lobe was then freed, and at necropsy, eight weeks after the pneumonolysis, it had reexpanded and practically filled the left hemithorax.

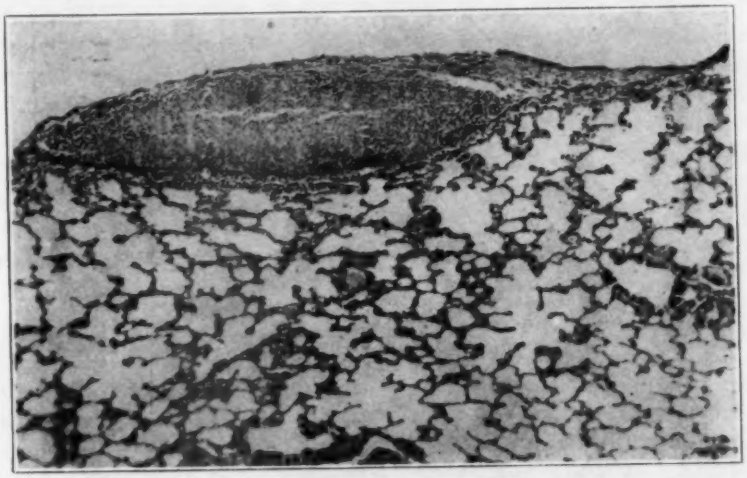

Fig. 6.—Low power photomicrograph of a typical adhesion produced by talc and iodine poudrage.

Fig. 7.—With addition of a Nicol prism showing the reaction is around the crystals of the talc powder.

In none of these animals was there found any evidence of bronchial obstruction, and the affected side was filled by mediastinal shift with which hernia of the opposite lower lobe was sometimes associated.

Of the 5 cats treated by the injection of a suspension of the powder into an artificial pneumothorax cavity, two showed no adhesions at two and three weeks

respectively, 1 showed marked mediastinal adhesions which made lobectomy difficult at the sixteenth day, and the other 2 had formed adhesions by the fourteenth and sixteenth day which made excision of the lower lobe impossible.

Adhesions were found after the injection of a suspension in isotonic solution of sodium chloride but not when sterile water was used.

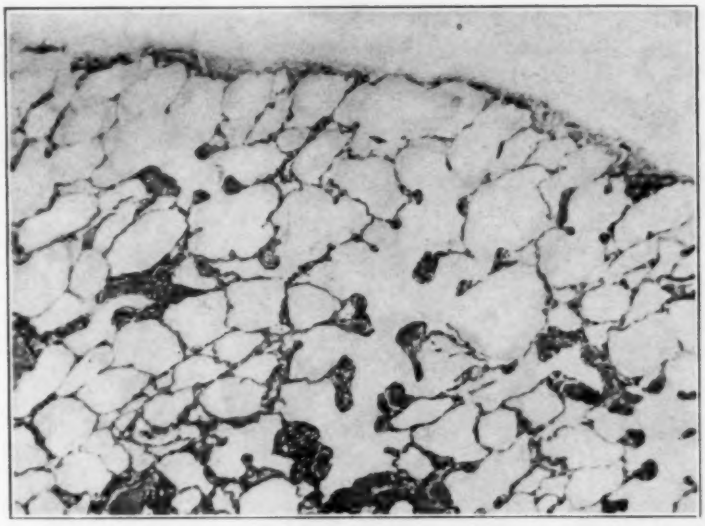

Fig. 8.—Photomicrograph showing typical emphysema.

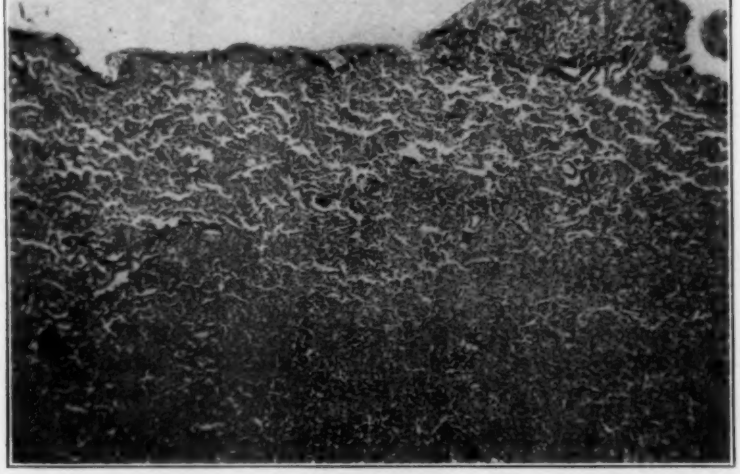

Fig. 9.—Photomicrograph showing typical collapse (same power magnification as in figure 8) taken from the same lobe at a distance of 1 cm., illustrating the effect of artificially produced adhesion on the expansion of the lung after lobectomy.

From these experiments there can be no doubt that with iodized talc poudrage: (1) adhesions can be produced but their situation and elasticity cannot be controlled; (2) the aseptic pleuritis produced gives rise to no ill effect on the parenchyma of the lung; (3) adhesions so produced are capable of causing dis-

tortion of the lung before operation and of causing collapse which may be permanent and complete in the remaining lung tissue of the same side after lobectomy. There is considerable difference of opinion regarding its use in man. Some surgeons hold that poudrage has greatly lessened the risk of postoperative collapse in their cases, while others consider it inadvisable because of the risk of empyema complicating the method and also because of the degree of thoracic deformity which follows when one side of the chest is not completely filled with lung tissue. For if pleural fusion is attained the remaining lobe cannot fill the normal hemithorax. The statistics of the two groups are not convincing in either direction, and it may be that the improvement of results of those in favor of poudrage is due to other factors.

As Churchill [1] has pointed out, the essential features to note are that pleural adhesions do not prevent a chronic progressive infection leading to fibrosis and collapse and that cases of bronchial obstruction with massive collapse are nearly always associated with adhesions to the wall of the chest. This suggests that in man the bronchial obstruction may be directly due to adhesions.

ANESTHESIA

The essentials of anesthesia for resection of a lung are the prevention of anoxia, the control of secretions and the abolition of reflex disturbance (Beecher [8]).

The following method is simple and satisfactory: A mixture of hydrochlorides of opium alkaloids (omnopon; pantopon) ⅓ grain (0.02 Gm.) and scopolamine 1/150 grain (0.4 mg.) are given one hour before operation, and the patient is then left in a darkened anesthetic room with a ½ grain (0.03 Gm.) decicain (tetracaine hydrochloride) lozenge in his mouth. Just before removal to the theater an intratracheal catheter of about one third the diameter of the trachea is passed with a laryngoscope and the preoperative medication is repeated together with administration of ephedrine. The patient is then placed in the lateral position on the table, which is tilted with a 10 degree slope, head downward, and as a spinal anesthetic 1:1,500 hypotonic solution of nupercaine hydrochloride is given. The intratracheal catheter is then connected with oxygen flowing at the rate of 2 liters a minute and attached to a valve so that a greater pressure than 1 cm. of mercury cannot occur. At a moment's notice the intratracheal catheter may be disconnected from the oxygen and attached to an electric aspirator which is kept in readiness. The intratracheal catheter is well tolerated, and besides supplying oxygen and being available for aspiration, it makes coughing ineffectual, thus preventing the dissemination of infected material in that way should flooding occur. Preoperative measures rarely empty a pathologic lobe of all its secretion. Since unfortunately bronchial tampons are difficult to insert and liable to displacement during the operation, reliance must be placed on intratracheal aspiration and posture to prevent the dangers of obstruction to the airway and the dissemination of septic secretions should flooding take place. It can be shown by injecting iodized oil into a lower lobe and placing the patient with that side uppermost in the position already described for lobectomy together with an intratracheal catheter in position, that dissemination is definitely less in the conscious patient than in one under general anesthesia. For at some period of general anesthesia there are irregular respiratory movements which do not occur in the conscious patient, and this is particularly so when the anesthesia has to be stopped to allow aspiration. The intratracheal oxygen prevents anoxia and does away with the risks of positive pressure anesthesia, such as impaction of secretions

in the smaller bronchi with subsequent atelectasis and infection and also the risk of alveolar rupture and the alteration of normal gaseous interchange due to failure of the expiratory muscles. It also avoids the manifold intricacies of controlled respiration and the danger involved in the lowering of the carbon dioxide content of the blood inherent in this method. This depletion of carbon dioxide so alters the dissociation curve of oxygen that a patient may appear to be of satisfactory color when definite tissue anoxia is present.

Marked increase of the carbon dioxide content of the blood also is deleterious, as it leads to cardiac irregularity and death from dilatation of the heart even when pure oxygen is being breathed (Crafoord [9]). The intratracheal administration of oxygen prevents lack of oxygen in the blood, even when both pleural cavities are open simultaneously, but in unawareness of the effect on the alkali reserve of the blood of prolonged open pneumothorax when intratracheal oxygen is being administered, the following experiments were performed: Six cats were anesthetized with intraperitoneally administered pentobarbital sodium. The left side of the chest was kept wide open for three hours in 4 cases and for two and a half hours and one hour in the other 2 animals, while oxygen was given intratracheally at a rate of 2 liters a minute and at a pressure not above 1 cm. of mercury. Blood was taken from the left ventricle at once and at regular periods afterward, and no alteration in alkali reserve was found, though 2 animals were subjected to total pneumonectomy, 2 previously had had single lobes removed and 2 had simple thoracotomies. Two further animals were tried. One was deliberately and grossly overdosed with anesthetic and died shortly after the three hour period with a 30 per cent rise in the alkali reserve. The other animal died at two and three-quarter hours with the same findings, but it had had both lower lobes removed and the upper lobe of the left lung was completely fibrosed, so it had considerably less functioning lung tissue than would occur in an operation on man.

A local anesthetic is never injected into the hilar region, for evidence is accumulating that paralysis of the vagal branches to the lung may tend toward postoperative pulmonary edema, especially if fluids are given intravenously (Farber [10]). O'Shaughnessy [11] showed that blocking the vagus at the hilus did not abolish cardiac irregularity, and Edwards [12] found no evidence of hilar reflexes and demonstrated that their alleged effect was produced by mechanical obstruction through torsion of the main pulmonary artery. Certainly there has never been any need to invoke such reflexes to account for the condition of the patient in any operation I have seen.

OPERATIVE STAGE

Operation should be performed after midday, so that any accumulation of secretions can be expectorated during the morning. The importance of this in pulmonary tuberculosis has long been known (Allen [13]), and I believe it applies equally whenever there is the complication of excessive sputum.

During the operation it is rare to find anything like a complete fissure dividing a pathologic lobe from its neighbors, and the separation is best carried down to the hilus by incision and immediate closure. Blunt dissection lacerates the lung and makes suture more difficult and so increases the risk of bronchopleural fistula,

9. Crafoord, C.: J. Thoracic Surg. **9**:237, 1939.
10. Farber, S.: Neuropathic Pulmonary Edema: Further Observations. Arch. Path. **30**: 180 (July) 1940.
11. O'Shaughnessy, L.: J. Thoracic Surg. **5**:386, 1936.
12. Edwards, R.: Brit. J. Surg. **27**:392, 1939.
13. Allen, D.: J. Thoracic Surg. **4**:76, 1934.

with its attendant alterations in intrapleural pressure and with the formation of a pathway for the spread of infection in either direction.

The method of dealing with the hilus must reduce the incidence of such fistulas to a minimum. Also, it must not produce more than a minimal reaction in the bronchus, especially if the upper lobe is being excised, for fear of obstructing the main stem bronchus. And, finally, care must be taken in the ligature of the blood vessels, as occlusion of a large branch of the pulmonary artery running to another lobe is easy and may lead to fibrosis in its area of supply, while sepsis in the pulmonary vein may lead to retrograde thrombophlebitis and collapse of the adjacent lobe. Fifteen lobectomies have been performed on cats and the effects studied from a few hours to six months after operation. Some were performed by individual ligation; some, by mass ligature, and others, by various combinations, and in this small series the results were equally satisfactory whatever the method employed. In man dissection of the pedicle with the application of a clamp is to be avoided unless suture is possible well proximal to the clamp, as crushing of the cartilage usually leads to fistula formation. It would appear from the careful work of Blades [14] that individual ligation is the best method so far devised. But if this is not practicable, then the tourniquet must be resorted to, and it should not be placed too close to an adjacent lobe for fear of occluding branches of the pulmonary artery running to it. Inflammatory reaction is limited by placing as few sutures as possible in the stump before removing the tourniquet. If speed is essential, the application of two tourniquets on the proximal side allows first one to be loosened and tied and then the other without the necessity of any sutures. Sloughing does not appear to take place, and fistula is rare after this procedure.

The phrenic nerve should not be interrupted during the operation, as this interferes both with inspiration and with the reciprocal innervation of the muscles used in coughing and so further lessens the power of expectoration in a chest already suffering from lack of adequate intercostal movement consequent on thoracotomy. Phrenicectomy also predisposes to collapse by increasing the intrapleural pressure (Haight [15]).

On the evidence already presented I suggest that any adhesions found running to the remaining lung tissue after lobectomy be carefully scrutinized and sectioned if it appears that by their contraction they will distort the bronchus or lead to irregular expansion of the lobe. I have had 1 man whose case I think illustrates this point. At the removal of the lower lobe of the left lung great care was taken not to divide the adhesions running from the upper lobe to the diaphragm. After operation the lobe appeared to be pulled downward and expansion took place from below up and was not complete for about fifteen weeks.

Lobectomy is an operation which is difficult to perform without soiling the operative field; so antiseptics are frequently employed. As the effect of many of these substances on the pleura and the subjacent lung was unknown, the following experiments were performed to ascertain if they had any relation to postoperative collapse.

1. One cubic centimeter of a 1:1,000 aqueous solution of euflavine was injected into the pleural cavity of rats. Necropsy was performed at varying periods up to ten weeks, and no histologic change was found. The dye staining was no longer visible to the naked eye after a fortnight.

14. Blades, B., and Kent, E. M.: J. Thoracic Surg. **10**:84, 1940.
15. Haight, C., and Deegan, J. K.: Am. Rev. Tuberc. **25**:197, 1937.

2. Ten milligrams of sodium sulfathiazole in 10 per cent solution in isotonic solution of sodium chloride was injected into the pleural cavity of normal albino rats 100 to 150 Gm. in weight. A slight pleural effusion formed at once but was reabsorbed in forty-eight hours, and no histologic change was found at autopsy from the second to the fourteenth day. If large doses were given, pleural effusions rapidly formed and the animals died with cyanosis and dyspnea.
3. Ten milligrams of sulfathiazole in a 10 per cent suspension in 6 per cent acacia in isotonic solution of sodium chloride showed a slight pleural effusion for four days, but otherwise no change.
4. Sulfapyridine in the same dosage and in a similar suspension produced no definite effect to the naked eye or on biopsy up to seventeen days from injection.
5. Neither the rats given injections of the suspending medium nor the controls showed any change.

From this I think it may be inferred that euflavine in normal concentrations does not affect the pleura or the lung, that sulfathiazole and sulfapyridine are also innocuous in average doses but that the former should not be placed in the pleural cavity in large quantities as it causes massive effusion, though not so readily as does sodium sulfathiazole. I always use cloths wrung out in euflavine solution to protect the edges of the wound, but I have never at operation placed any of the sulfonamide compounds in the pleural cavity, as the organisms found in putrid empyema due to opening of the bronchus are not affected by this group of drugs. This form of empyema may lead to collapse from fibrosis of the visceral pleura, which is rare in other septic infections if they are adequately drained.

Drainage is not a necessity after lobectomy, but I feel that it is like Moynihan's hypnotic stitch; the surgeon sleeps the better for its use and the patient need in no way be inconvenienced by it. If in some cases the surgeon feels that it can be dispensed with, I think it is advisable to leave a little sodium citrate solution in the pleural cavity to retard coagulation, for in cases in which clot forms aspiration is difficult and usually ineffectual and more adequate drainage has to be established. The site of drainage should be posterolateral, and it should not be dependent, as this leaves a long sinus track when the diaphragm rises. I have found intercostal drainage satisfactory, and there is no need with modern methods of dealing with the hilus to insert the tube more than just through the wall of the chest.

POSTOPERATIVE STAGE

The tube should be attached to an apparatus so that known definite degrees of negative pressure can be maintained in the thorax during normal respiration but so that forceful expiration and coughing will take place against a known definite positive pressure.

The importance of this is obvious on reflection on the mechanism of removal of material through the respiratory passages. Ciliary action and respiratory movement aid, but coughing is the essential way. The tussive squeeze forces secretions into the larger bronchioles, and from those of 1 mm. in diameter or over the bechic blast, which is formed by the sudden opening of the glottis following a rapid increase of intrathoracic pressure, forces a column of air from the alveoli

to the exterior (Archibald and Brown [16]; Carlson and associates [17]). Thus if the tube is attached to an apparatus which keeps a persistent subatmospheric pressure, not only will coughing be rendered ineffective on that side, but matter in the bronchi will tend to be forced peripherally into the smaller respiratory passages, giving rise to collapse.

This subatmospheric pressure should not be increased to any great extent with the hope of completing the expansion of a partially collapsed lobe even many weeks after operation. A patient of mine responded well to this treatment and expansion appeared to be 80 per cent, when he suddenly collapsed and died in a few minutes. Postmortem examination showed that death was due to spontaneous pneumothorax of the opposite lung, on the anterior border of which were found numerous emphysematous bullae, though none were present on the side of operation. In this case the negative pressure had been gradually increased to 5 cm. of mercury in a period of about six weeks.

On return to the ward the patient is placed at once in Fowler's position. This, in spite of the spinal anesthesia, appears to be the most comfortable posture, and it also has the advantage of being the best both for drainage of the upper lobe bronchus and of the pleural cavity.

The oxygen tent is used for the first few days, more on account of the equitable temperature and freedom from draughts and air-borne infection which are possible with the modern thermostatically controlled machine than because of need of oxygen. In fact, oxygen should be used sparingly, as it increases the viscosity of the bronchial secretions, so making their elimination more difficult (Holinger [18]).

Coughing is encouraged, and it is not painful if manual support is given to the ribs. Breathing exercises, which have been learned before the operation, are commenced as soon as possible, with the object of increasing the respiratory movements of the affected side. Regular and systematic persuasion in coughing, expectoration and breathing exercises is most important, and opiates should be withheld until the patient has satisfactorily cleared his throat. Inhalations of 5 per cent carbon dioxide aid considerably. Should retention of secretions occur in spite of this, aspiration either by an intratracheal catheter or through the bronchoscope should be resorted to. In such cases chemotherapy with a sulfonamide compound is indicated, and it should also be employed and in large doses if pulmonary infection takes place, when the drug may be given by insufflation through the bronchoscope as well as by mouth. In some clinics bronchoscopic aspiration is carried out as a routine on completion of lobectomy; this may be of value when general anesthesia has been used, but I have never seen the need of it with a conscious patient operated on under spinal anesthesia. Neither have I found the bronchodilator effect of amyl nitrite (Nicholson [19]) of any obvious value in helping to get rid of secretions and to increase aeration of the lung; it has been tried in only 3 cases.

CONCLUSIONS

Bronchial obstruction and pulmonary infection and fibrosis are the important causes of collapse of the lung after lobectomy. Clinically they present as obstructive

16. Archibald, E., and Brown, A. L.: Cough: Its Action on Material in Tracheobronchial Tract; Experimental Study, Arch. Surg. **16**:322 (Jan) 1928.

17. Carlson, H. A.; Ballon, H. C.; Wilson, H. M., and Graham, E. A.: J. Thoracic Surg. **2**:573, 1933.

18. Holinger, P.; Basch, F. P., and Poncher, H. G.: Influence of Expectorants and Gases on Sputum and Mucous Membranes of Tracheobronchial Tree, J. A. M. A. **117**:675 (Aug. 30) 1941.

19. Nicholson, W. F.: J. Thoracic Surg. **9**:194, 1939.

massive collapse and as chronic progressive pneumonia with subsequent diffuse fibrosis.

The avoidance of pulmonary infection is the most important measure in the prevention of postlobectomy collapse.

Iodized oil appears to have no definite relation to postlobectomy collapse, save that it may give rise to lipid pneumonia.

Production of adhesions cannot be accurately controlled; even if successfully produced they cannot prevent the two common forms of collapse from occurring, and, finally, adhesions have been shown to cause postlobectomy collapse. For these reasons, their artificial production should be abandoned, and adhesions found at operation should be sectioned if they are likely to give rise to distortion of the remaining lung tissue.

The simplicity and the safety of spinal anesthesia with intratracheal oxygen are noted.

The importance of attaching the drainage tube to an apparatus which maintains a negative intrapleural pressure but allows coughing to take place against a positive pressure is stressed.

Prof. H. N. Green gave assistance in this study and allowed me to work in his department. Dr. H. E. Harding gave continual help; Prof. G. A. Clark allowed Mr. P. D. Greaves to do numerous estimations of the alkali reserve in his department; Dr. J. Rennie, medical officer of health, and Dr. J. Clark, medical superintendent, gave me permission to publish clinical cases.

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ROENTGENOLOGIC DEMONSTRATION OF SPINAL METASTASES FROM LEIOMYOSARCOMA OF THE UTERUS

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BOSTON

Leiomyosarcoma of the uterus is a relatively rare tumor, representing not more than 2 per cent of uterine leiomyomas.[1] [Miller and Rogers,[2] in a study made at the Massachusetts General Hospital covering fifty years (1876-1926), found an incidence of 1.4 per cent.] They also described a case in which metastasis to the hip

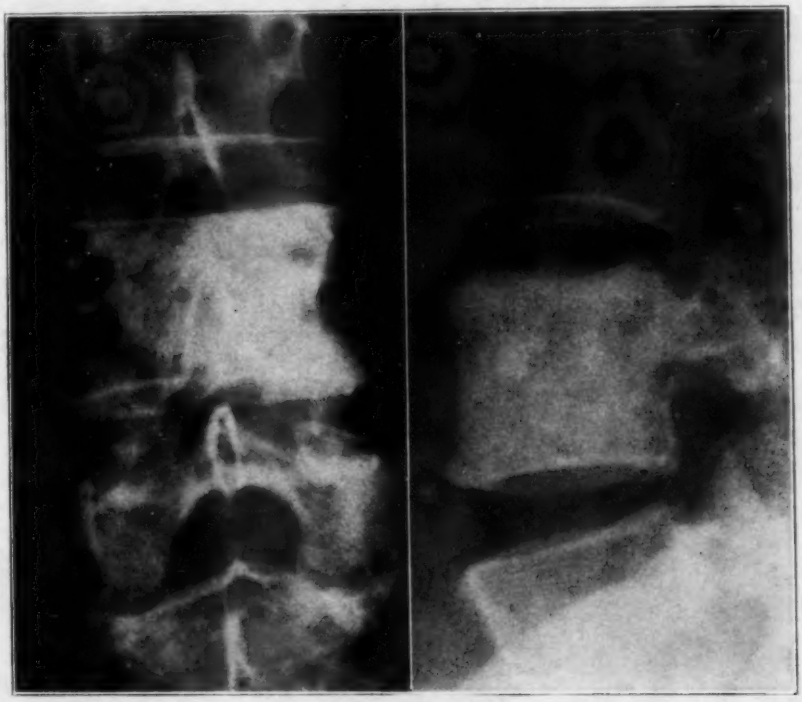

Fig. 1 (case 1).—Roentgenograms showing osteoblastic metastasis to the fourth lumbar vertebra approximately five years after hysterectomy. There is a certain similarity in appearance to the metastasis shown in figure 3, without quite as fine detail as is seen in the latter.

caused spontaneous fracture. Metastasis from leiomyosarcoma is even more rare than the primary tumor. Because the roentgenographic appearance of osteoblastic metastasis from leiomyosarcoma has received little if any emphasis in the published reports, 2 cases in which this diagnosis was proved are presented.

From the Department of Radiology, Massachusetts General Hospital.

1. Wheelock, M. C., and Warren, S.: Leiomyosarcoma of the Uterus, Ann. Surg. **116**: 882, 1942.

2. Miller, R. H., and Rogers, H.: Sarcoma of the Uterus, New England J. Med. **198**: 927, 1928.

REPORT OF CASES

CASE 1.—A 46 year old district nurse was first seen at the Massachusetts General Hospital in 1935 because of pain in the back and several palpable masses in the abdomen and

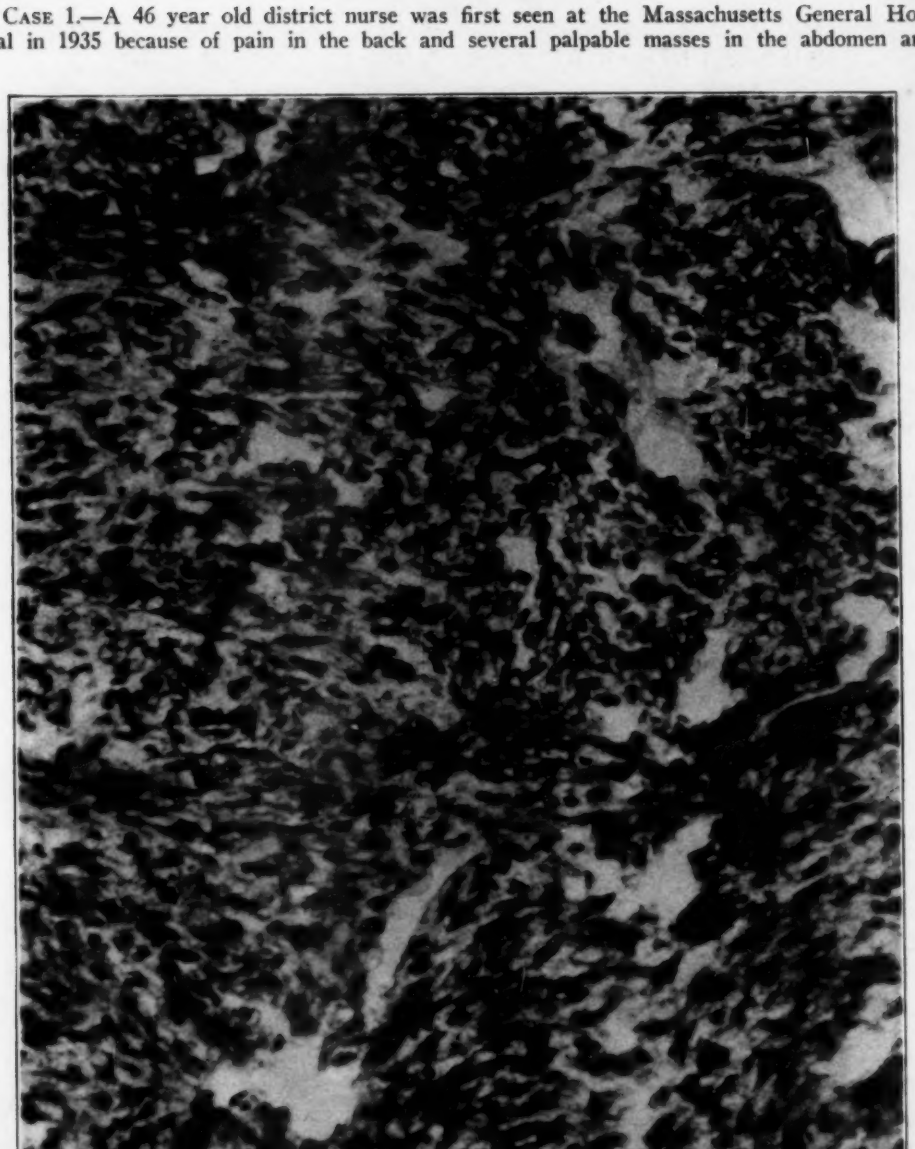

Fig. 2 (case 1).—Photomicrograph (section from fourth lumbar vertebra) showing leiomyosarcoma.

pelvis. Three years before, a total hysterectomy had been performed in another hospital, and an intramural leiomyosarcoma had been found. During the investigation of the cause of her pain, a roentgenogram of the abdomen revealed increased density of the fourth lumbar vertebra (fig. 1), as well as definite deformity of the psoas shadows.

From 1935 to 1941 an extremely large amount of roentgen treatment was administered to various areas; on one occasion a radiation ulcer in the left upper quadrant of the abdomen was excised. The roentgenographic appearance of the fourth lumbar vertebra gradually changed, revealing progression of the destructive lesion, until by 1940 the vertebra had almost entirely collapsed. At this point a spinal fusion was done, and biopsy of material obtained from the fourth lumbar vertebra confirmed the diagnosis of metastatic leiomyosarcoma.

In December 1941 a cordotomy was performed for intractable pain; metastatic nodules in the chest were demonstrated by roentgenogram. The patient's final admission was in February 1942. She died the following April, slightly more than ten years after the original operation (hysterectomy) for leiomyosarcoma. Autopsy revealed metastatic leiomyosarcoma involving the liver, lungs and spine. The changes in the fourth lumbar vertebra were originally thought to represent osteoblastic metastasis, and in view of the history of removal of

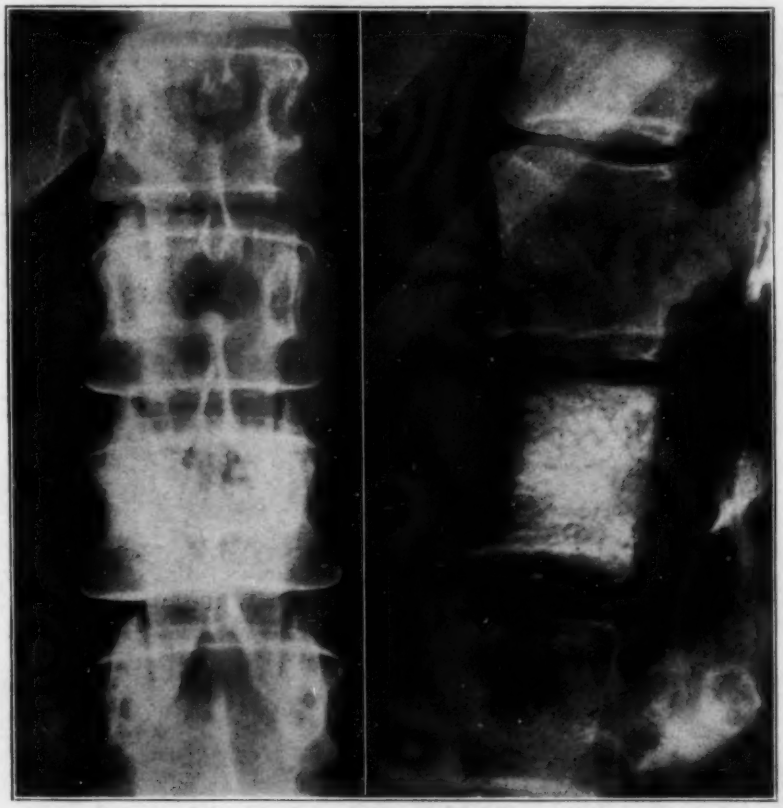

Fig 3 (case 2).—Localized roentgenograms of the second lumbar vertebra demonstrating the osteoblastic metastasis. Note the increased density of the second lumbar vertebra. Irregular lines of diminished density are seen in the pathologic area involving the posterior two thirds of the vertebra.

a leiomyosarcoma this tentative diagnosis was made; it was later confirmed histologically, both by biopsy and by necropsy (fig. 2).

Comment.—Inasmuch as the appearance of the bone is the point of importance in this report, the amount of roentgen therapy, the technic by which it was given and the various areas treated have not been described in detail. Although the various masses which were treated showed definite improvement under roentgen therapy, and this is remarkable considering the type of tumor involved, the bone lesion progressed slowly but steadily until the body of the fourth lumbar vertebra was almost completely destroyed.

The roentgenologic appearance of the metastatic involvement of the bone in case 1 led to the diagnosis in the following case.

CASE 2.—A 50 year old woman entered the Massachusetts General Hospital in June 1943 for study of pain in the lower part of the back, radiating down both legs. The pain was of

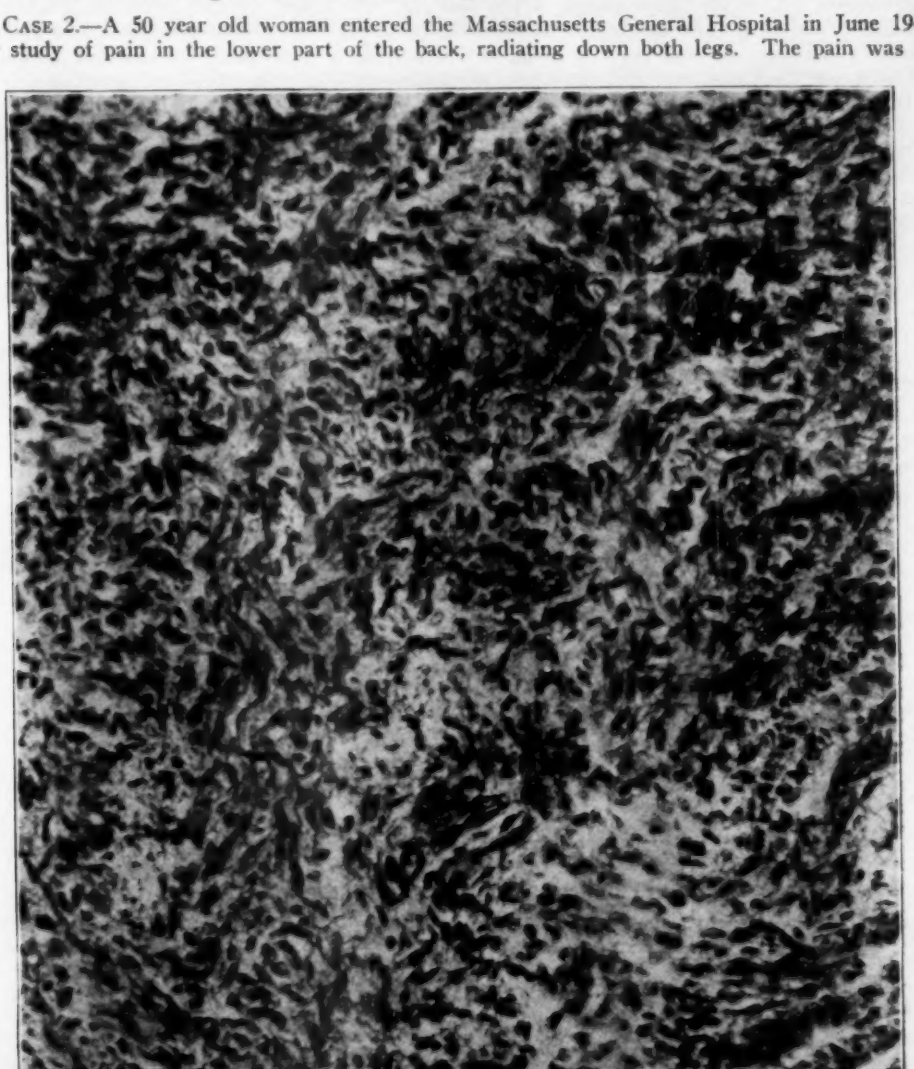

Fig. 4 (case 2).—Photomicrograph (section from tumor in the spinal canal overlying the second lumbar vertebra) showing leiomyosarcoma.

one month's duration and had come on suddenly about forty-eight hours after the patient had jumped from a height of approximately 2 feet (60 cm.). At another hospital, investigation of the cause of the pain revealed an abnormal second lumbar vertebra. The patient was given a small amount of roentgen treatment, which did not, however, relieve her pain.

The past history was noncontributory, except that an operation "for fibroids," at which part of the uterus and the left ovary and the left tube were removed, had been performed one year previous to her admission to this hospital.

The presence of a lesion in the second lumbar vertebra was established (fig. 3) and was interpreted as a sign of metastasis from a malignant tumor. An examination of the lumbar portion of the spinal canal with iodized poppyseed oil revealed a complete block just below the upper margin of the third lumbar vertebra. At operation a large mass of tumor was found protruding into the bony canal. Its main portion was over the body of the second lumbar vertebra, but it also extended above and below for a few centimeters. The histologic report was "metastatic leiomyosarcoma" (fig. 4).

Comment.—Although a specimen of bone could not be obtained for biopsy, it seems likely that the tumor in the spinal canal and that in the bone were of the same type because of their close proximity, and that they in all probability arose from the uterine tumor.[1]

COMMENT

When the appearance of the roentgenograms of the vertebrae in the 2 cases is compared, a certain similarity is seen. In case 2, there is increased density surrounding irregular linear shadows which suggest the possibility of vascular channels, although this cannot be ascertained definitely. In case 1, it is seen that there is rather diffuse increased density but that there are poorly defined areas of rarefaction within this density. The linear shadows are not visualized as they are in case 2, but are suggested. Except for the irregular lines seen in the diseased areas there is no recognizable difference from any other form of osteoblastic metastasis. The roentgenograms in case 2 were taken with a rotating anode tube, and the peculiar pattern is particularly well demonstrated. It is possible that had the roentgenograms in case 1 been taken with a tube of corresponding focal spot they might have shown more resemblance to this appearance.

It is not believed that the present status of roentgenology allows a definite etiologic differentiation of osteoblastic metastasis. However, the peculiar pattern shown in case 2 has not been previously described or recognized so far as can be determined. The diagnosis may be suspected when there is a history of hysterectomy or of preceding leiomyosarcoma of the uterus, and if roentgenologic study reveals a focus of metastatic malignant growth. It is understood that osteoblastic metastases may be produced by other malignant uterine tumors.

There was osteoblastic metastasis in both of the 2 cases presented. This type of metastasis, in contradistinction to the osteolytic form, may possibly be explained on the basis of the relatively slow growth of the tumor. It may spread by way of the vertebral veins,[3] as carcinoma of the prostate so commonly does.

SUMMARY

Attention is called to the fact that osteoblastic metastasis may be produced by leiomyosarcoma of the uterus.

Two cases in which there was proved metastasis from leiomyosarcoma of the uterus to the lumbar portion of the spine are reported, and their roentgenologic appearance is described.

These cases are published with the permission of Drs. W. J. Mixter and C. G. Mixter.

The Massachusetts General Hospital.

3. Batson, O. V.: The Function of the Vertebral Veins and Their Role in the Spread of Metastasis, Ann. Surg. **112**:138, 1940.

GERMICIDAL ACTIVITY OF ALCOHOL, HYDROCHLORIC ACID AND ALUMINUM POTASSIUM SULFATE

THEIR EFFECT ON CUTANEOUS FLORA

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It is generally thought that the skin is able in some manner to destroy bacterial organisms with which it comes in contact. This ability has been referred to as the "self-disinfecting power of the skin" by Arnold and his co-workers [1] (1930).

Colebrook [2] (1930) observed the disappearance of exogenous bacteria from the surface of normal skin and suggested that it may be due to (1) desiccation, (2) activity of a lysozyme or (3) concentration of salts of sweat. He believed that neither desiccation nor lysozyme is an important factor but that concentration of salts of sweat may be a factor. Bryan and Mallmann [3] (1933) expressed the opinion that desiccation plays an important role, as did also Norton and Novy [4] (1931). Meleney [5] (1927) stated that the bactericidal action of sweat and of sebaceous glands is of relatively little importance. Usher [6] (1928) showed that sweat is a good culture medium.

Arnold (1930) and Sharlit and Scheer [7] (1923) found the superficial layers of the skin to be acid and to have a p_H of 5 to 5.7. Marchionini and Hausknecht,[8] Marchionini, Schmidt and Kiefer [9] (1938) and Marchionini and Schmidt [10] (1939)

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9. Marchionini, A.; Schmidt, R., and Kiefer, J.: Säuremantel der Haut und Bakterienabwehr: Ueber die regionäre Verschiedenheit der Bakterienabwehr und Desinfektionskraft der Hautoberfläche, Klin. Wchnschr. **17**:736, 1938.

10. Marchionini, A., and Schmidt, R.: Säuremantel der Haut und Bakterienabwehr: Der Bakteriengehalt in pathologischen Lücken des Säuremantels, Klin. Wchnschr. **18**:461, 1939.

reported on the acid-base conditions of the skin. They pointed out that diseased areas show a higher bacterial count and are more alkaline than normal areas. They have also shown that the cutaneous surface is acid if sweat is allowed to evaporate, but if this is prevented the ammoniacal products which are formed cause an alkaline reaction. Pillsbury and Shaffer [11] (1939) also tested the p_H of the skin and made similar observations.

Bernstein and Hermann [12] (1942) found that the p_H of the hands was 3.5 to 5.8, of the groins 5.5 to 6.3, of the areas between the toes 5.5 to 6.5 and of the armpits 6.5 to 8.0. They reported an increase in acidity when the temperature was high, indicated by a decrease in the p_H from 5.8 to 4.0.

Davletov [13] (1940) published an article in Russian which later was translated into English and published in the *Bulletin of War Medicine* (1942). In it are reported his observations on the effect of acid on the bacterial flora of the skin. He found that a 0.1 per cent solution of hydrochloric acid is an effective disinfecting agent for surgeons' hands and that the bactericidal power is further enhanced by the addition of 20 per cent to 40 per cent of "surgical spirit."

The methods for obtaining material for study of the bacterial flora of the skin and the effect of germicidal agents on it have mostly consisted of swabbing, scraping and cutting sections of skin for culture and impression. It is difficult to secure quantitative results with any of these methods.

Price [14] in 1938 published a new quantitative method of studying the bacterial flora of the skin, which consisted of scrubbing the hands and arms with brush, soap and water in fourteen consecutive basins. Later Price [15] (1939) adapted this method to the study of the effectiveness of ethyl alcohol, mercury bichloride, potassium iodide and Harrington's solution for the disinfection of the skin. He concluded that when properly used a solution containing exactly 70 per cent by weight of ethyl alcohol is the most effective of all for preoperative preparation of the hands and arms.

Pohle and Stuart [16] (1940, 1941) used a modification of the Price technic in the study of cleaning agents, rosin and fatty acid rosin soaps.

Cromwell and Leffler [17] (1942) reported experiments using Pohle and Stuart's modification. They found that aluminum and potassium sulfate in 10 per cent aqueous solution, though not germicidal, gives as good a "bacterial destruction curve" as a 70 per cent solution of alcohol.

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11. Pillsbury, D. M., and Shaffer, B.: Cutaneous Reaction with Reference to the Surface p_H, the Reaction to Ointments and Solutions of Different p_H and the Effect of the Skin in Modifying the p_H of Applied Solutions, Arch. Dermat. & Syph. **39**:253 (Feb.) 1939.

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16. Pohle, W. D., and Stuart, L. S.: (*a*) The Germicidal Action of Cleaning Agents: A Study of a Modification of Price's Procedure, J. Infect. Dis. **67**:275, 1940; (*b*) The Germicidal Activity of Rosin Soap and Fatty Acid Rosin Soap as Indicated by Hand Washing Experiments, Oil & Soap **18**:2, 1941.

17. Cromwell, H. W., and Leffler, R.: Evaluation of "Skin Degerming" Agents by a Modification of the Price Method, J. Bact. **43**:51, 1942.

Kronig and Paul [18] (1897) first showed that the germicidal efficiency of acids is proportional to the hydrogen ion concentration of their solutions. Winslow and Lochridge [19] (1906) showed that a 0.0077 normal solution of hydrochloric acid will produce a 99 per cent reduction in the number of Escherichia coli in forty minutes.

Beyer [20] (1911) and Gregersen [21] (1916) compared solutions containing exactly 70 per cent of alcohol by weight with solutions containing 70 per cent by volume. Both workers concluded that the solution containing 70 per cent by weight is superior as a germicide in vitro. Price [15] (1939) reported that in using his method 70 per cent by weight proved to be the most efficient concentration of alcohol. Pohle and Stuart [16a] (1940) also found this solution to be an efficient agent when the technic of Price was used.

Alum has always been regarded as a powerful astringent, and its most important use today is as a local astringent. There are few references to its antiseptic properties. According to Miquel,[22] it will inhibit the multiplication of bacteria in the proportion of about 1 part in 200.

It may be assumed from the literature cited that a low p_H is a factor in the self-disinfecting power of the skin. It is also known that hydrochloric acid is an efficient germicide in vivo and in vitro. Cognizant of the existence of these two factors, we decided to apply the technic outlined by Price, to evaluate quantitatively the effect of a 0.5 per cent solution of hydrochloric acid on the bacterial flora of the hands and arms and to compare it with the effect of a solution containing 70 per cent of alcohol by volume and that of a 10 per cent solution of aluminum and potassium sulfate. We also wished to estimate the bacterial flora of the hands and arms after the wearing of rubber gloves.

METHOD

The basins were wrapped in paper and sterilized in the autoclave. Fourteen were generally used in each experiment. One thousand to 1,500 cc. of distilled water was placed in each basin. Surgeons' scrub brushes were wrapped and sterilized in the autoclave. A white toilet soap was used throughout the experiments. Surgeons' rubber gloves were powdered, wrapped in a towel and sterilized in the autoclave.

One minute was used as the period of washing at each bowl. Exactly ten seconds was allowed for soaping the brushes, hands and arms; then the hands and arms were scrubbed for thirty-five seconds. The brush was then dropped into the basin, and the soap was rinsed off the hands and arms for fifteen seconds. This same procedure was repeated at each wash basin. In experiments in which test solutions were used, they were applied after seven minutes of scrubbing with soap and water. A piece of sterile gauze was used, and the hands and arms were sponged for two minutes. Then scrubbing was again resumed for a period of seven minutes.

One cubic centimeter of wash water from each basin was placed in a sterile Petri dish, and liquefied agar was poured in, thoroughly mixed with the sample and allowed to harden. Plates were incubated for forty-eight hours at 37 C. The bacteria were then counted and

18. Kronig, B., and Paul, T.: Die chemischen Grundlagen der Lehre von der Giftwirkung und Desinfection, Ztschr. f. Hyg. **25**:1, 1897.

19. Winslow, C.-E. A., and Lochridge, E. E.: The Toxic Effect of Certain Acids upon Typhoid and Colon Bacilli in Relation to the Degree of Their Dissociation, J. Infect. Dis. **3**:547, 1906.

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21. Gregersen, J. P.: Untersuchungen über die desinfizierende Kraft der desinfizierenden Stoffe in Verhältnis zu ihrer Konzentration, Zentralbl. f. Bakt. (Abt. 1) **77**:168, 1916.

22. Miquel, in Wood, H. C., and others: The Dispensatory of the United States of America, ed. 22, Philadelphia, J. B. Lippincott Company, 1937.

the totals calculated. In preparing the curves we used the method of Pohle and Stuart; that is, the bacterial count per basin was plotted as the abscissa and the basin number as the ordinate.

Sterile rubber gloves were used in a series of experiments and were worn for one hour. They were put on the hands after the application of the test solution and subsequent drying with a sterile towel. A solution containing 70 per cent of alcohol by volume, a 0.5 per cent solution of hydrochloric acid (0.137 normal) and a 10 per cent solution of aluminum and potassium sulfate were the test solutions used in these experiments.

RESULTS

The results given in the following tables are averages of from four to eight individual tests. Curves were plotted from these results.

TABLE 1.—*Normal Procedure*

Experiments	Bacterial Counts per Basin in Thousands													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Soap and water scrubbing	4,580	4,675	4,164	3,355	3,270	2,658	2,257	2,320	1,547	1,738	1,563	1,137	1,053	821
2. Distilled water scrubbing *	3,674	4,194	2,445	2,372	2,090	1,796	1,622	1,260	1,224	1,350	948	..	..	..

* Eleven basins were used in this series.
1. Results plotted in chart 1.
2. Results plotted in chart 2.

TABLE 2.—*Test Solutions*

Experiments (Soap and Water in All Basins)	Bacterial Counts per Basin in Thousands														
	1	2	3	4	5	6	7		8	9	10	11	12	13	14
3	4,054	3,740	3,221	2,940	2,636	1,898	1,560	Hydrochloric acid, 0.5%; 2 min. *0	23	29	38	38	40	51	62
4	3,608	4,084	3,359	1,859	2,034	1,592	1,433	Alcohol, 70% by vol.; 2 min. *0	0	12	15	18	16	10	12
5	9,600	6,210	5,640	3,990	3,180	2,940	1,628	Potassium alum, 10%; 2 min. *448	358	224	315	289	330	357	310

* Bacterial count per cubic centimeter of test solution.
3. Results plotted in chart 3.
4. Results plotted in chart 4.
5. Results plotted in chart 5.

TABLE 3.—*Test Solutions Plus the Wearing of Rubber Gloves*

Experiments (Soap and Water in All Basins)	Bacterial Counts per Basin in Thousands														
	1	2	3	4	5	6	7		8	9	10	11	12	13	14
6	7,787	5,422	4,610	2,810	2,767	2,542	2,267	Gloves worn for 1 hour	2,842	2,520	2,475	2,222	2,047	2,092	1,350
7	5,788	5,512	4,918	3,609	3,250	2,233	2,178	Hydrochloric acid, 0.5%; 2 min.; gloves 1 hour *0	403	501	409	495	438	408	438
8	6,062	5,008	3,636	4,075	3,310	3,287	2,709	Alcohol, 70% by vol.; 2 min.: gloves 1 hour *0	21	27	29	22	28	20	23
9	7,650	7,830	7,695	5,085	4,860	3,820	3,105	Potassium alum, 10%; 2 min.; gloves 1 hour *930	1,845	2,280	2,025	2,835	1,890	2,395	2,385

* Bacterial count per cubic centimeter of test solution.
6. Results plotted in chart 6.
7. Results plotted in chart 7.
8. Results plotted in chart 8.
9. Results plotted in chart 9.

COMMENT

We found that the numbers of organisms removed from the hands and arms in the soap and water series and the distilled water series were reasonably similar. From the curve shown in chart 2 it appears that the first period of scrubbing is required to loosen the epithelium and remove fat. Maximum removal of bacteria is delayed until the second period. This delay is not as apparent for the scrubbing with soap and water (chart 1). There is also a much more gradual decrease after the second basin in the distilled water series. This observation differs from those of Price, who found that brushing the skin without soap reduces the basic flora more rapidly than does the use of soap.

In the group of hand washing experiments in which test solutions were used, we found alcohol in a concentration of 70 per cent by volume to be a highly efficient germicidal agent for the flora of the skin. The removal curve in chart 4 illustrates the effect.

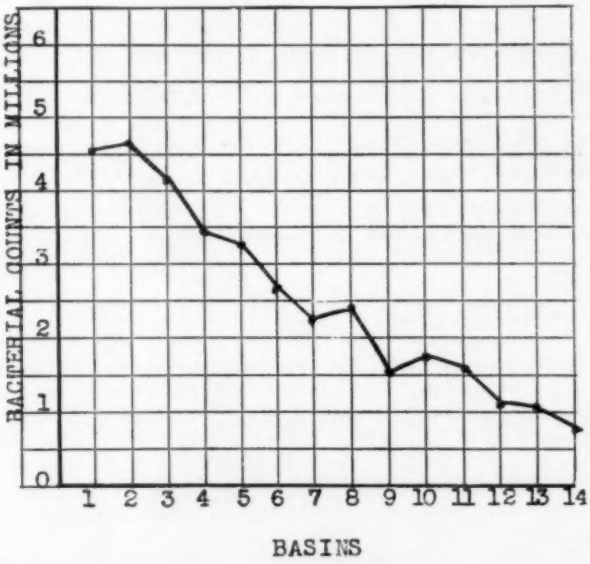

Chart 1.—Removal curve of scrubbing with soap and water.

A 0.5 per cent solution of hydrochloric acid was also found to be a highly efficient germicidal solution. Davletov [13] found that a 0.1 per cent solution was an efficient disinfecting agent for the skin, but we obtained more favorable results with a 0.5 per cent solution. The solution was not irritating to the skin of any volunteer. In fact, the skin was extremely soft and smooth during the time this solution was being used in our experiments. The removal curve in chart 3 shows 0.5 per cent hydrochloric acid to be an efficient germicidal agent for the resident flora of the skin.

A 10 per cent solution of aluminum and potassium sulfate proved rather efficient in reducing the bacterial flora of the skin but was not as effective as alcohol or hydrochloric acid. We agree with Cromwell and Leffler [17] that it does give a good "bacterial destruction curve," as is apparent in chart 5.

In the series of experiments in which rubber gloves were used, the first group served as the control. The subjects scrubbed the hands with soap and water in seven basins, wore rubber gloves for one hour and then scrubbed in seven additional

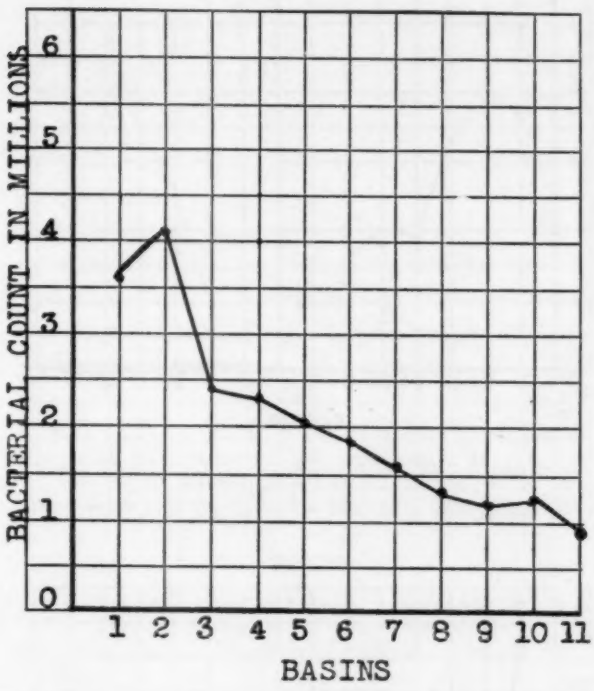

Chart 2.—Removal curve of scrubbing with distilled water.

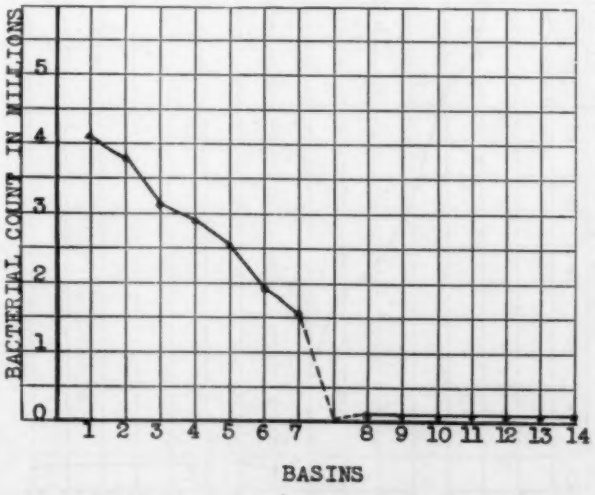

Chart 3.—Removal curve of a procedure which included scrubbing with soap and water in the first seven basins, application of a 0.5 per cent solution of hydrochloric acid for two minutes and scrubbing with soap and water in the last seven basins.

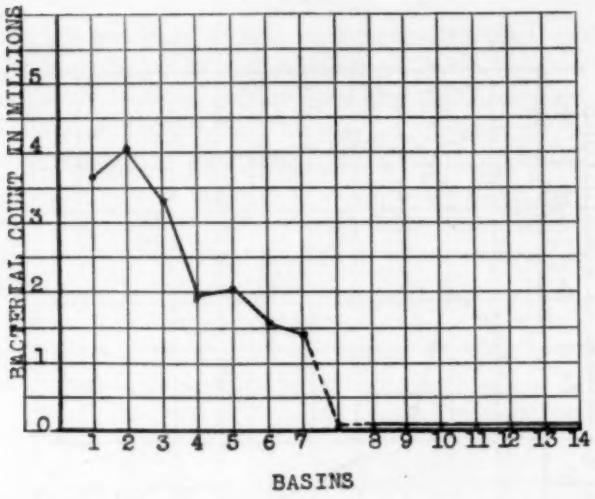

Chart 4.—Removal curve of a procedure which included scrubbing with soap and water in the first seven basins, application of a solution containing 70 per cent of alcohol by volume for two minutes and scrubbing with soap and water in the last seven basins.

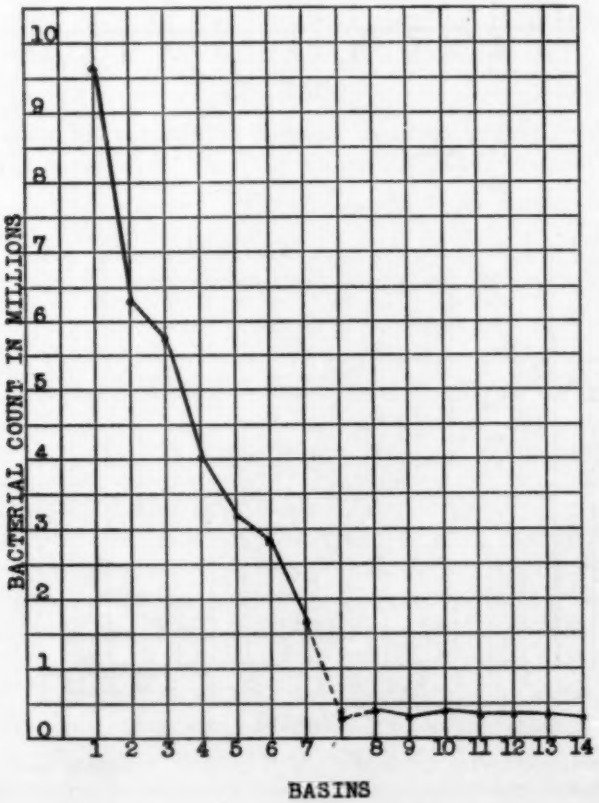

Chart 5.—Removal curve of a procedure which included scrubbing with soap and water in the first seven basins, application of a 10 per cent solution of aluminum and potassium sulfate for two minutes and scrubbing with soap and water in the last seven basins.

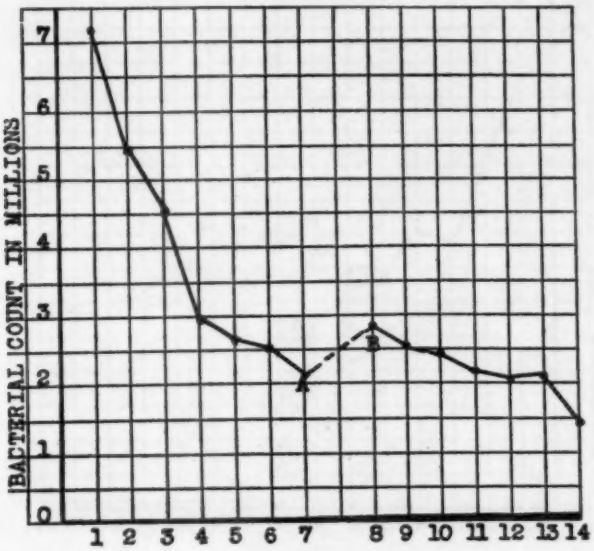

Chart 6.—Removal curve of a procedure which included scrubbing with soap and water in the first seven basins, wearing sterile rubber gloves for one hour and scrubbing with soap and water in the last seven basins. The dotted line *A-B* represents the interval during which rubber gloves were worn.

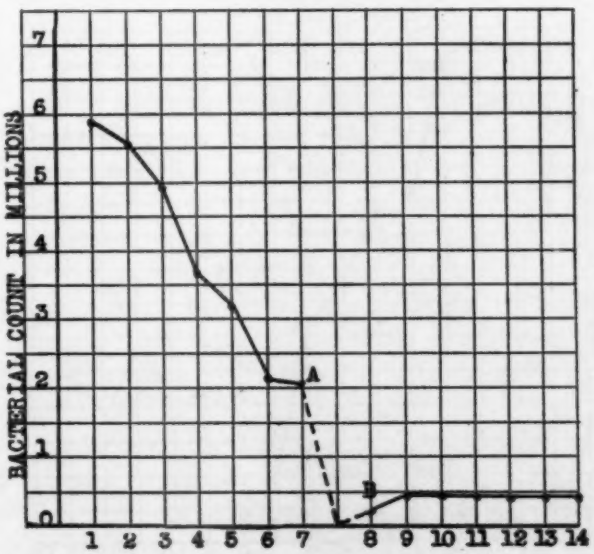

Chart 7.—Removal curve of a procedure which included scrubbing with soap and water in the first seven basins, application of a 0.5 per cent solution of hydrochloric acid for two minutes, wearing sterile rubber gloves for one hour and scrubbing with soap and water in the last seven basins. The dotted line *A-B* represents the interval during which rubber gloves were worn.

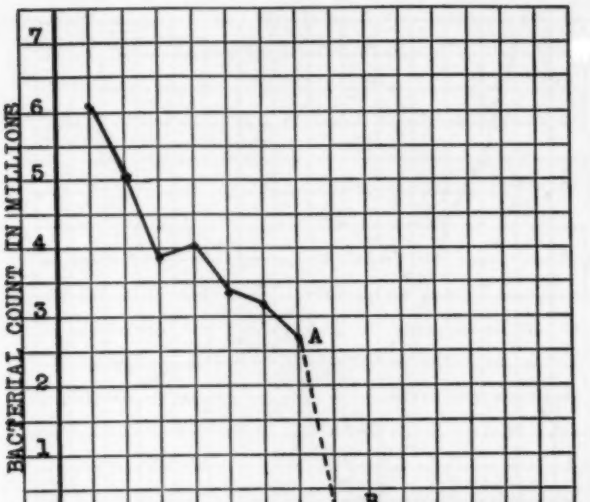

Chart 8.—Removal curve of a procedure which included scrubbing with soap and water in the first seven basins, application of a solution containing 70 per cent of alcohol by volume for two minutes, wearing sterile rubber gloves for one hour and scrubbing with soap and water in the last seven basins. The dotted line *A-B* represents the interval during which rubber gloves were worn.

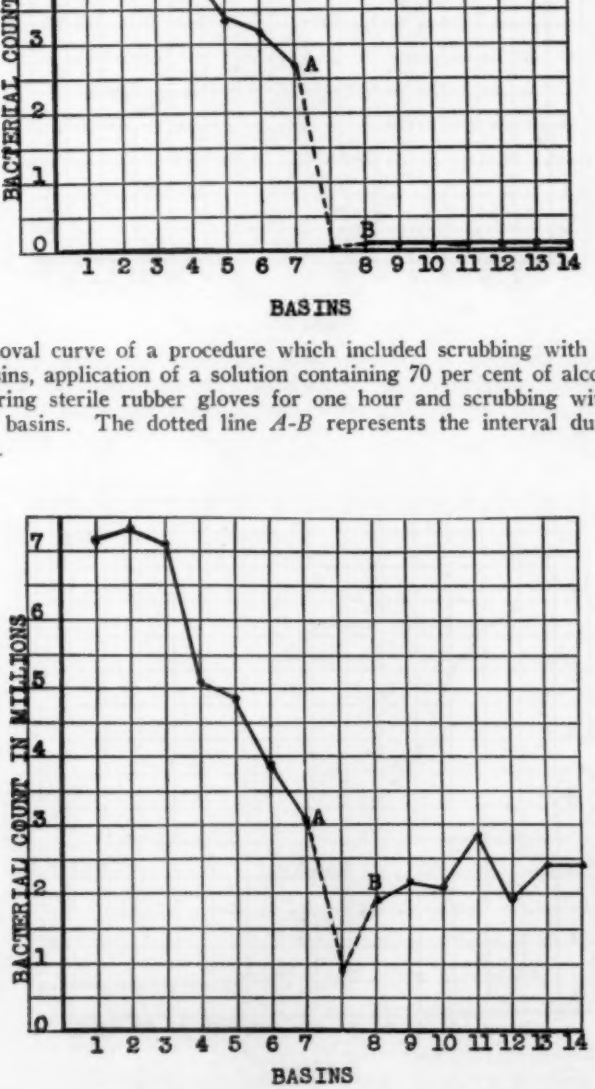

Chart 9.—Removal curve of a procedure which included scrubbing with soap and water in the first seven basins, application of a 10 per cent solution of aluminum and potassium sulfate for two minutes, wearing sterile rubber gloves for one hour and scrubbing with soap and water in the last seven basins. The dotted line *A-B* represents the interval during which rubber gloves were worn.

basins. The results of these experiments are given in table 3. We found that after rubber gloves had been worn for one hour the bacteria were more numerous than after the regular scrubbing with soap and water. By comparing chart 1 with chart 6 one may readily observe this effect.

When a 70 per cent solution of alcohol was used prior to the wearing of the rubber gloves, the bacterial counts rose only slightly, as is seen in table 3 and in the curve in chart 8.

When a 0.5 per cent solution of hydrochloric acid was used prior to the wearing of the rubber gloves, the bacterial counts rose somewhat higher than those in the alcohol series. However, it still was efficient when compared with the soap and water used in the control experiments. The results are plotted in chart 7.

When a 10 per cent solution of aluminum and potassium sulfate was used prior to the wearing of the rubber gloves, the bacterial counts rose and were much like those of the control, except that as the astringent action was overcome by the scrubbing, the counts became higher, as indicated in the ninth to the fourteenth basin. The results are plotted in chart 9.

CONCLUSIONS

Alcohol in a concentration of 70 per cent by volume was found to be an efficient germicidal agent for the bacterial flora of the skin when used as outlined in these experiments.

A 0.5 per cent solution of hydrochloric acid was found to be highly efficient also but not entirely comparable to the alcohol.

Aluminum and potassium sulfate in 10 per cent aqueous solution evidently hardens the skin to such an extent that the organisms are imprisoned but not killed. They may be released after the softening of the skin which occurs when rubber gloves are worn and then removed in the subsequent scrubbing.

We believe that either alcohol 70 per cent by volume or hydrochloric acid 0.5 per cent is sufficiently efficient to use in the presurgical preparation of the surgeon's hands and that a 0.5 per cent solution of hydrochloric acid could safely be used so as to conserve the supply of alcohol for more essential purposes.

We believe that a 0.5 per cent solution of hydrochloric acid has a true germicidal action on the bacterial flora of the skin.

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PRIMARY TUBERCULOSIS OF THE SPLEEN

REPORT OF A CASE

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Hepatosplenomegaly is a very significant finding in an abdominal examination and often leads to a study of the entire gamut of differential diagnoses. The more common causes of this interesting change are sufficiently well catalogued to show tuberculosis as an infrequent offender. However, because of its obscurity and its amenability to treatment, tuberculosis of the spleen forms a worthy chapter in the study of the surgical splenopathies.

Intelligent understanding of this disease dates back to Winternitz'[1] work. According to Winternitz, and this has been substantiated by most subsequent writers, tuberculosis of the spleen is not a primary disease in the strict pathologic sense. Evidence of earlier tuberculous infection was found in all his autopsies. However, as a clinical entity the disease may be considered primary. In the spleen, tuberculosis may form an active focus for systemic infection. In this respect splenic tuberculosis is analogous to renal tuberculosis, which is secondary to some healed or inactive focus elsewhere but may act independently as a nidus of infection. The factors which determine the pathologic patterns in splenic tuberculosis are:[1] (1) the general reaction of the spleen to acute infection, manifested as hypertrophy and engorgement, (2) the specific lesions due to the tubercle bacilli and their localization and (3) the reparative process of the tissue after injury.

In the acute form of the disease, hypertrophy and engorgement are most pronounced, and the specific lesion may be slight if the course is rapid. Generally the specific lesion is more evident.

In the chronic productive form, fibrosis will predominate over splenic hypertrophy and tubercle formation. The common picture is that of a healing process vying with tuberculous activity, the result being a huge spleen which shows sclerocaseous changes.

Clinically three types of disease can be recognized.[2] In the acute type the infection is overwhelming and the spleen is enlarged and soft, with an engorged pulp. In the subacute form the spleen is larger and firmer, with pronounced tuberculous nodules. In the chronic form the spleen is very large and may be calcified; there are adhesions to the surrounding viscera. The incidence of the disease is greatest between 20 and 40 years of age. The acute type is characterized by high fever, profuse sweats and acute splenic tumor. In the chronic disease there are pain in the left upper quadrant of the abdomen, gastrointestinal disturbances, anorexia, lassitude, anemia, loss of weight and fever. On physical examination the spleen is always enlarged and may be nodular and hard. The liver and super-

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This paper is published with the approval of the Veterans Administration, which, however, does not assume responsibility for the opinions expressed or the conclusions drawn by the authors.

1. Winternitz, M. C.: Tuberculosis of Spleen, Arch. Int. Med. **9**:680-697 (June) 1912.

2. Frank, T. J.: Primary Tuberculosis of Spleen, Roy. Melbourne Hosp. Clin. Rep. **10**: 113-118, 1939.

ficial lymph nodes may be enlarged. Winternitz [1] observed hepatic involvement in 80 per cent of the cases in which the liver was examined. Involvement of lymph nodes was present in 57 per cent of his cases. There may be tuberculous involvement in other parts of the body. In the same series 40 per cent of the patients showed evidence of pulmonary tuberculous disease. In 16 per cent the lesions were healed, and in 24 per cent they were active. The laboratory examinations should include a complete study of the blood, roentgenograms of the chest and the abdomen and biopsy of enlarged lymph nodes. The results of studies of the blood are nonspecific. Polycythemia, thrombopenic purpura, hemolytic anemia and Banti's anemia have been described.[2] Weiner and Carter [3] reported a case of acute thrombopenic purpura with miliary tuberculosis of the spleen in which recovery followed splenectomy.

The treatment of this disease is splenectomy. An enlarged liver and involved lymph nodes or inactive peritoneal tuberculosis are no contraindication, according to Frank.[2] Hickling [4] reported 2 cases in which there was roentgen evidence of miliary tuberculosis. The patients recovered, and the signs of involvement of the chest disappeared after splenectomy. Solomon and Doran [5] report a case in which the patient showed involvement of the liver and the inguinal lymph nodes but recovered after splenectomy.

The rationale of splenectomy, then, is to remove an active focus of tuberculous infection and prevent further hematogenous spread. While the literature contains reports of cures in the presence of extrasplenic tuberculosis, our attitude is not so sanguine. We do feel, however, that considerable benefit can be derived from splenectomy and that the indications should merely postulate a spleen that can be demonstrated as the seat of active disease.

We wish to add our experience in the diagnosis and treatment of a case of splenic tuberculosis.

REPORT OF CASE

It was difficult to secure a good history from this patient, a Negro 47 years of age. He was admitted to the Veterans Hospital Dec. 15, 1941, complaining of vertigo and weakness. He also had dyspnea and cough. While at home the patient had complained of sweats and fever and had lost 20 pounds (9 Kg.) in weight. His appetite was poor, and he had occasionally observed blood in his stools. He said he had not had syphilis, gonorrhea or malaria. The duration of symptoms could not be determined.

On examination the patient appeared to be poorly nourished and chronically ill but fairly well developed. Examination of the neck revealed several hard, fixed, matted supraclavicular lymph nodes on the left side. The chest was resonant throughout. The breath sounds were normal, no rales were heard and there was normal fremitus. Examination of the heart showed the point of maximum intensity to be in the fifth interspace in the midclavicular line. The sounds were of good quality. Numerous extrasystoles were present, and the rate was rapid. Blood pressure was 130 systolic and 70 diastolic. The radial arteries were thickened. The edge of the liver could be felt four fingerbreadths below the right costal margin. It was firm and smooth. The spleen was decidedly enlarged, extending down to the iliac crest, and it was hard and nodular. A reducible hernia in the right inguinal region was present.

A blood count at the time of the patient's admission to the hospital showed 1,600,000 red cells and a hemoglobin content of 34 per cent. The total number of white cells was 12,200, with 64 per cent polymorphonuclears. There were 58 segmented cells, 6 stab cells, 31 lymphocytes, 3 monocytes, 1 eosinophil and 1 basophil. The sedimentation rate was 135.

3. Weiner, J. J., and Carter, R. F.: Acute Thrombocytopenic Purpura Hemorrhagica Associated with Miliary Tuberculosis of Spleen: Recovery with Splenectomy, Ann. Surg. **113**:57-61, 1941.

4. Hickling, R. A.: Tuberculous Splenomegaly with Miliary Tuberculosis of Lungs, Quart. J. Med. **7**:263-269, 1938.

5. Solomon, H. A., and Doran, W. T., Jr.: Primary Tuberculosis of Spleen, New York State J. Med. **39**:1288-1295, 1939.

The stools were found to contain occult blood. The icterus index was 5. Plasmodium malariae could not be found in the blood. Urinalyses gave essentially normal results. Agglutination tests for typhoid, paratyphoid, typhus and undulant fever gave negative results. Cultures of the stools for typhoid, paratyphoid and dysentery were negative.

Retrograde urography was performed to determine whether the mass in the left upper quadrant of the abdomen was an enlarged kidney. Pyelograms showed evidence of distortion and displacement of the left kidney due to extrinsic pressure. A specimen of the patient's urine was injected into a guinea pig, but tuberculosis was not found at autopsy of the animal. The initial roentgenogram of the chest appeared normal.

While in the hospital the patient exhibited a hectic febrile course. He complained of lack of appetite and of weakness. In view of the cervical lymphadenopathy, the hepatosplenomegaly and the febrile course, a presumptive diagnosis of tuberculosis of the spleen was made. On Jan. 16, 1942, a supraclavicular lymph node on the left side was excised. It

Fig. 1.—Microscopic section showing tuberculosis of a lymph node from the left supraclavicular region. Giant cells are clearly seen.

was found to be tuberculous. This strengthened the presumption of tuberculosis of the spleen. The report of the pathologist, Dr. Henry S. Blank, was as follows:

Gross Appearance.—The specimen consisted of a lymph node about the size of a small hickory nut. It measured 3 by 2.5 by 1.8 cm. The organ appeared to have been removed intact. The capsule was smooth and presented a slight degree of cyanosis. On section the node manifested increased resistance. The cut surface was pinkish white, with a slight yellowish mottling which suggested infiltration by a malignant or tuberculous process.

Microscopic Appearance.—The section was that of a lymph node presenting considerable distortion of the normal architectural pattern. The capsule was fairly well preserved. The remainder of the node had been completely destroyed by a necrotic and fibrotic process. In several areas the focal necrosis was characteristic of tuberculosis, and occasionally typical tubercle formation was observed. Numerous Langhans giant cells were seen. Except at isolated points just under the capsule, where a diffuse sprinkling of lymph, monocytoid and plasma cells was noted, the remainder of the section was acellular. A diagnosis of tuberculosis was made.

The patient was given a transfusion of 500 cc. of whole blood on January 24, January 30 and February 6. The hemoglobin content of his blood rose to 59.5 and the red cell count to 3,000,000. On February 7, laparotomy was performed by Dr. Coffee.

Operation.—A rectus incision was made on the left side. The fascia was divided in the line of incision and the left rectus muscle split in the line of its fibers. The abdomen was explored manually. The spleen was studded with white nodules and was considerably enlarged. A splenule the size of a walnut was located at the hilus of the spleen and contained several caseating nodules. The spleen was attached to the lateral parietal peritoneum and the diaphragm by filmy adhesions. The tail of the pancreas was located between the posterior surface of the hilus of the spleen and the anterior surface of the left kidney. Both kidneys were normal to palpation. The liver was enlarged 3 fingerbreadths below the costal margin. There was a nutmeg appearance of the surface, and there were some areas of capsular fibrosis. There was no evidence of nodulation or caseation in the liver. The stomach, the large and small intestine and the peritoneum appeared normal. The spleen was freed from

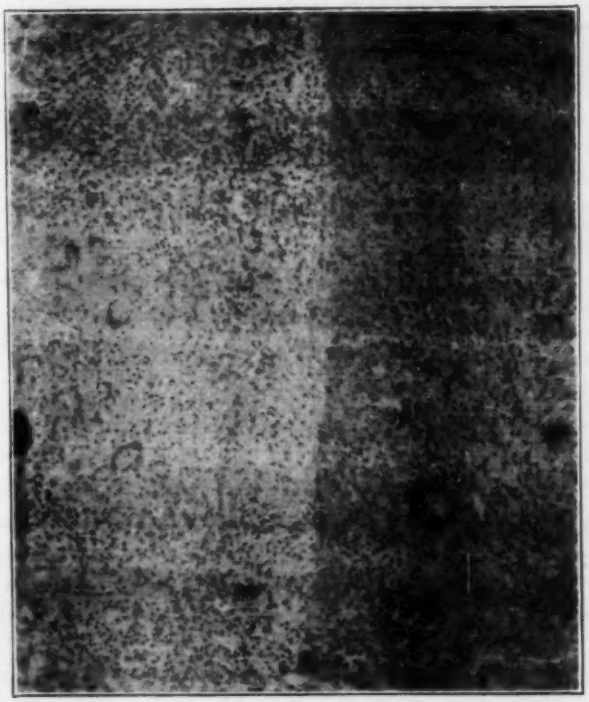

Fig. 2.—Microscopic section showing tuberculosis of spleen. Giant cells are clearly seen.

adhesions to the left lateral parietal peritoneum and diaphragm by blunt dissection with the fingers. It was thereby mobilized, rotated medially and delivered into the wound. The gastrolienal ligament was clamped, cut and ligated. The splenic pedicle was then doubly clamped, cut and ligated. The tail of the pancreas was carefully separated from the under surface of the spleen. The spleen was thereby severed from all its abdominal connections and removed. Oozing from various divided adhesions was controlled with hot packs, and the wound was closed in layers. The skin was closed with dermal sutures and three silk retention sutures were inserted.

The report of the pathologist on the surgical specimen was as follows:

Gross Appearance.—The specimen consisted of a very large spleen measuring 21 by 16 by 10 cm. The external surface was noticeably hemorrhagic, and the gross contour of the organ was distorted by a nodular formation. The splenic capsule was irregularly thickened, cyanosed and hemorrhagic. Numerous white subcapsular areas were noted. On section, the organ seemed to be involved by a caseofibrotic process which grossly appeared to be tuberculous. The process seemed to originate in numerous focal areas and to radiate from these

areas in all directions. Each focus of infection produced nodular deformation of that portion of the spleen. The intervening splenic tissue was beefy red, with considerable intervening edema and the gross appearance of interstitial hyperplasia.

Microscopic Appearance.—The section consisted of a portion of spleen presenting a definite distortion of the normal architectural pattern. Large areas of the tissues had undergone necrosis with adjacent infiltration by round cells and Langhans giant cells. The appearance of the process was typically that of tuberculosis. A diagnosis of tuberculosis of the spleen was made.

The postoperative course was stormy, with high fever, profuse perspiration, malaise and anemia. The patient was treated with repeated transfusions, adequate diet, vitamins and ultraviolet radiation to the abdomen and neck. From July 9 until August 5, the date of his discharge from the hospital, he was ambulatory and completely afebrile. He did, however, exhibit persistent tachycardia, and the hemoglobin content of his blood never rose above 79 per cent, with a red cell count of 4,140,000. Ultraviolet radiation to the neck resulted in a noticeable diminution in the size of the lymph glands. During the patient's postoperative bouts of fever, roentgenograms of the chest were made, but no evidence of miliary tuberculosis was present. The patient gained 13 pounds (6 Kg.) in weight. Although it was felt that he

Fig. 3.—Samples of temperature range before and after splenectomy.

would benefit by further care in a sanatorium, he did not desire extended hospital treatment and therefore was discharged.

The patient's condition was considered improved. The presence of tuberculosis in the liver was never demonstrated, and the tuberculosis of the glands in the neck was considered to have subsided. Attempts to communicate with the patient by mail for follow-up were unsuccessful.

SUMMARY

A brief review of the essential nature of primary tuberculosis of the spleen is presented.

Splenectomy is the means of removing an active focus of tuberculous infection and preventing further hematogenous spread.

We present a report of a case of tuberculosis of the spleen in which improvement followed splenectomy.

Supportive therapy in the form of transfusions, adequate diet, vitamins and ultraviolet radiation is an important adjunct to surgical treatment.

Veterans Administration Facility.

PROGRESS IN ORTHOPEDIC SURGERY FOR 1942

A REVIEW PREPARED BY AN EDITORIAL BOARD OF THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS

VIII. AMPUTATIONS, APPARATUS AND TECHNIC

PREPARED BY J. WARREN WHITE, M.D., GREENVILLE, S. C.

Amputations.—Literature pertaining to war surgery continues to be extensive as one would expect, and as was the case last year many articles on amputation have appeared. Nothing has been published this year, however, that has been on as high a technical or literary plane as those contributions mentioned in "Progress in Orthopedic Surgery for 1941." A somewhat similar but much briefer compendium was published as War Memorandum No. 5 by the Medical Research Council of the British War Wounds Committee [223] during this last year and deserves mentioning as much for its brevity as for the practical information it contains. Nothing particularly new is emphasized, except possibly that consultation with an associate should be required before amputation is performed. The type of amputation should depend on (*a*) the time elapsed since the injury, (*b*) the level of the injury and (*c*) the general condition of the patient. This article has served as a pattern for others of the same nature. Two of the five members of this Subcommittee on Amputations have written separate articles, each enlarging somewhat on his phase of the subject, and one of these will be mentioned shortly. The two controversial subjects, end bearing and nerve treatment, were not discussed in this official government publication, and it is evident that the last word on these two points has not been said. When a British authority like Gordon-Taylor [224] maintains that a nerve should be cut squarely across and not pulled down, ligated or subjected to injections, while the newly appointed Surgeon General of the Army,[225] a long time authority on amputations, in an excellent article advocates just the opposite, the occasional amputator is justifiably considerably confused and might therefore conclude that it does not make much difference, except under certain conditions. An example of such a condition is a high tibial amputation, in which the retraction and cutting of a nerve would be likely to place the inevitable terminal neuroma in a weight-bearing location. The value of the so-called guillotine operation in severe compound injuries requiring amputation is extolled by all authors,[226] if operation is delayed twenty-four hours and performed so as to make a concave surface and avoid the distressing "lead pencil" stump. Traction on skin is universally insisted on. Kirk [225] calls attention to the ease of doing a late plastic closure when a guillotine amputation had been performed an average of four months before.

Another controversial point about amputations is the treatment of the end of the bone. Kirk [225] states that the bone should be sawed through without doing anything to the periosteum except to traumatize it as little as possible and cut it completely around—not sew it over the end or skin it back, as was advocated

223. Emergency Amputations, Medical Research Council War Memorandum no. 5, abstracted, War Med. **2**:147-153 (Jan.) 1942.

224. Gordon-Taylor, G.: Ten Commandments in Amputation, Lancet **1**:669 (June 6) 1942.

225. Kirk, N. T.: Amputations in War, J. A. M. A. **120**:13-16 (Sept. 5) 1942.

226. Footnote 223. Gordon-Taylor.[224] Kirk.[225]

formerly. Schmorell [227] advocates the covering of bone surfaces with periosteum, admittedly with sound physiologic reasoning, except that there is always a suture line of the periosteum, and there is no guaranteeing that an osteophyte will not grow there.

[Ed. Note.—One of the editors (J. W. W.) feels that this is an unnecessary requirement and unjustifiably prolongs an operation in which time is frequently so valuable.]

Seven articles on the use of refrigeration in amputations have been reviewed,[228] which is an indication of the growing popularity and interest of this relatively new technical method in amputations. Nothing new has been brought out, except that fear of frostbite damage to skin is unjustified in view of a case report by McElvenny,[228f] for whose patient, a 70 year old man, refrigeration was employed for twenty-eight days without ill effect. For those wishing to try this anesthetic agent, the specifications of an efficiently functioning refrigeration box have been published by Gordon.[228e] This method is obviously still in the experimental stage, but progress is definitely being made. It is satisfactory that so many surgeons are interested, in order that a safe practical technic may be worked out for occasional amputators, as so many surgeons are. The value of real refrigeration for intractible pain, particularly of the extremities, is being emphasized by this investigative work, and its local application with ethyl chloride is discussed by two British authors.[229] These authors claim that immediate relief has been obtained in various diseases of the soft tissues, from de Quervain's tenosynovitis to pain in the lower part of the back.

[Ed. Note.—These articles must be read reservedly, but they do call attention to a therapeutic agent that heretofore has been little used. No damage is done by judicious, temporary superficial freezing of the skin. As an office "stunt" for certain impressionable patients with a low pain threshold, one can imagine it to be of considerable and at least temporary value. To many, it might smack a little of empiricism, but occasions for its use might appear sufficiently often to justify having a tube or so in the office.]

Thorek [230] has described for a low thigh amputation a technic simulating a guillotine procedure, except that sufficient bone is removed to permit end closure in layers without drainage after careful hemostasis. A tourniquet is not used, since the femoral vessels are accessible for easy ligation when the circular incision is made just above the knee after the inner hamstrings are cut. This amputa-

227. Schmorell, H.: Covering of Bone Surface in Stumps of Long Bones with Periosteum, Zentralbl. f. Chir. **68**:1912-1913 (Oct. 11) 1941.

228. (*a*) Allen, F. M.: Reduced Temperatures in Surgery: Experiments on Pelvic and Abdominal Refrigeration with Especial Reference to Traumatic and Military Surgery, Am. J. Surg. **55**:451-466 (March) 1942. (*b*) Crossman, L. W.; Ruggiero, W. F.; Hurley, V., and Allen, F. M.: Reduced Temperatures in Surgery: Amputations for Peripheral Vascular Disease, Arch. Surg. **44**:139-156 (Jan.) 1942. (*c*) Schiebel, H. M.: Use and Evaluation of Anesthesia by "Freezing" for Surgery of Extremities in Diabetic Patients, North Carolina M. J. **3**:227-229 (May) 1942. (*d*) Crossman, L. W., and others: Refrigeration Anesthesia, Anesth. & Analg. **21**:241-254 (Sept.-Oct.) 1942. (*e*) Gordon, J. D.: Refrigeration Box for Amputation, Am. J. Surg. **58**:453-455 (Dec.) 1942. (*f*) McElvenny, R. T.: Present Status of Cooling Limbs in Preparation for Surgical Procedures, ibid. **58**:110-112 (Oct.) 1942. (*g*) Smith, W. E.: Refrigeration of Gangrenous Extremities Before Amputation, Ohio State M. J. **38**:826-829 (Sept.) 1942.

229. Henry, A. K.: Freezing with Ethyl Chloride to Relieve Pain and Loss of Movement, Lancet **2**:280-281 (Sept. 5) 1942. McIntosh, C. A., and Petrie, J. G.: Use of Ethyl Chloride Spray in Soft-Tissue Injuries, ibid. **2**:279-280 (Sept. 5) 1942.

230. Thorek, P.: Simplified Technic for Thigh Amputation, Surg., Gynec. & Obst. **75**: 225-228 (Aug.) 1942.

tion is more on the order of the Callander technic, which is discussed favorably by Brown,[231] who cites 21 consecutive operations without a postoperative death on patients ranging in age from 39 to 82. The one drawback to this amputation is its unpopularity with makers of artificial limbs, who ordinarily can fit a prosthesis better to a shorter stump.

During the last year, three more articles [232] on interinnominoabdominal amputations have been published, an indication that a few are still interested in this radical procedure. No new points are brought out that have not been thoroughly discussed in previous articles, and the procedure must be reserved for the rare and special cases fulfilling the rigid requirements for the consideration of such a radical operation.

Pack, McNeer and Coley [233] report a series of 31 consecutive cases of interscapulothoracic amputation for malignant tumor. Only 6 of the patients have survived. Although this very major surgical procedure has a greater usefulness than the interinnominoabdominal amputation, the need for its performance fortunately arises relatively seldom. One hundred and forty-one cases have been cited in the literature since 1900. The surgical technic originated by Berger, as well as those recommended by Kocher and by Littlewood, is discussed, but no radical modifications of any of these are advocated.

Surgical Technic.—Goodwin and Cameron [234] have reported success in using a pair of interdependent bone-holding forceps devised to aid in the open reduction of fractures and in maintaining apposition even in the oblique spiral fracture which is so common in the lower part of the tibia. Wire threaded through holes in the fragments drilled through the slotted jaws of the clamp maintains apposition with a minimum of material. The two supplementary instruments used for passing the wire loops through the hook arrangement are useful wherever wire or other material is to be passed through bone.

[ED. NOTE.—For surgeons partial to the use of wire for fixation, this instrument should be most useful.]

Farill [235] describes a subcutaneous method of lengthening the heel cord by using an especially devised knife which cuts the tendon longitudinally as well as transversely to make the Z tenotomy usually made at open operation. This is an ingeniously conceived procedure devised because of the difficulty in getting tendon elongation by alternate transverse incisions subcutaneously.

[ED. NOTE.—One of the editors (J. W. W.) recently published a description of a technic which has been employed for several years in which account is taken of the rotation of the heel cord. By judiciously placing the transverse subcutaneous incisions through two thirds of the cord at appropriate levels with an ordinary tenotome, the structure can be elongated without the longitudinal cut for which the special knife is necessary. In this way all the fibers are cut, and the tendon

231. Brown, J. R.: Low Thigh Amputation by Callender Method, M. Bull. Vet. Admin. **18**:237-240 (Jan.) 1942.

232. Morton, J. J.: Interinnomino-Abdominal (Hindquarter) Amputation, Ann Surg. **115**: 628-646 (April) 1942. Whittaker, A. H.: Interinnomino-Abdominal Amputation, Indust. Med. **11**:1-3 (Jan.) 1942. Whittaker, A. H., and Sobin, D. J.: Interinnomino-Abdominal Amputation, Ann. Surg. **115**:435-440 (March) 1942.

233. Pack, G. T.; McNeer, G., and Coley, B. L.: Interscapulothoracic Amputation for Malignant Tumors of Upper Extremity, Surg., Gynec. & Obst. **74**:161-175 (Feb.) 1942.

234. Goodwin, F. C., and Cameron, D. M.: Bone-Holding-Drilling Forceps, Southwestern Med. **26**:228-229 (July) 1942.

235. Farill, J.: Elongation of Achilles Tendon by Author's Technic in Therapy of Pes Equinus, Gac. méd. de México **72**:69-72 (Feb. 28) 1942.

gives way as would a manila rope if one had cut it partially through at different levels, making certain that all the strands were cut either above or below.]

Wassersug [236] has supplied a long felt want in suggesting a new marker for cutaneous localization which will be permanent and useful both for roentgen examination and surgical procedures. It is designed particularly, of course, for operations on the spine. A 1 per cent suspension of lampblack in iodized poppyseed oil is injected subcutaneously and intramuscularly where localization is needed.

Attention is called by Breck and Basom [237] to the value of a tourniquet on the leg when bone for grafting is removed from the tibia and cites the advantages of the Campbell-Boyd pneumatic tourniquet for this purpose.

[Ed. Note.—I have made use of this idea as have many others for years and suggest that it be employed when pinch grafts are needed for extensive burns in order to conserve blood in those usually extremely debilitated patients.]

Bell [238] justifiably advocates the use of alloy steel wire in general surgery, citing its various advantages but admitting that it is somewhat more difficult to use.

[Ed. Note.—Many, including Bunnell, who has used it particularly in operations on tendons, have advocated it for years, and it is felt that progress in orthopedic surgery will follow its more extensive use. Bell gives the name of the manufacturer.]

The early disappearance of kangaroo tendon used for repair of tendons as reported by Trethewie and Williams [239] discourages its use as suture material in tenoplasties and may serve to explain the poor results in many cases in which it has been used.

[Ed. Note.—As it has been frequently proved that good tendon repair takes place in four to six weeks, some doubt may arise relative to placing the blame on the kangaroo tendon material. The error probably frequently is due to inadequate original fixation. Silk seems to be the generally accepted material in such instances. It is much easier to handle; the knots are more likely to hold, and it is permanent.]

The importance of only three weeks' immobilization in tenodeses is advocated by Kernwein.[240] As a result of animal experimentation, he has found that after three weeks prolonged protection retards the development of tensile strength.

[Ed. Note.—This seems to be a little short in view of reports of similar experiments, and it is felt that adding another week would do no particular harm.]

The fact that unfavorable reaction of the tissues to dissimilar alloys is not simply due to electrolytic action but to the physical and chemical properties of the metals themselves is discussed by Bothe and Davenport.[241] They state that solubility and the degree of toxicity of the dissolution products appear to be the

236. Wassersug, J. D.: New Marker for Spine Surgery, J. Bone & Joint Surg. **24**:464-465 (April) 1942.

237. Breck, L. W., and Basom, W. C.: Use of Campbell-Boyd Pneumatic Tourniquet for Spine Fusion Procedures, J. Bone & Joint Surg. **24**:461 (April) 1942.

238. Bell, R. H.: Impressions Concerning Use of Alloy Steel Wire in General Surgery, Mil. Surgeon **91**:185-187 (Aug.) 1942.

239. Trethewie, E. R., and Williams, E.: Use of Kangaroo Tendon for Muscle and Tendon Suture, Australian & New Zealand J. Surg. **11**:207-208 (Jan.) 1942.

240. Kernwein, G. A.: Study of Tendon Implantations into Bone, Surg., Gynec. & Obst. **75**:794-796 (Dec.) 1942.

241. Bothe, R. T., and Davenport, H. A.: Reaction of Bone to Metals: Lack of Correlation with Electrical Potentials, Surg., Gynec. & Obst. **74**:231-235 (Feb.) 1942.

chief factors. They consider that such constituents as nickel, copper or manganese are toxic and should be avoided. They feel that vitallium comes near to meeting the requirements for a nonirritating substance but hope the rarer metal tantalum will be even better after it has been given a trial.

Venable,[242] in discussing factors in the choice of material for bone plates and screws, advises avoidance of the use of plaster whenever possible, implying that its mere use unnecessarily prolongs convalescence.

[ED. NOTE.—It is feared that statements of this nature by an enthusiast for internal fixation are too prone to influence surgeons less experienced in open technic, to the detriment of their patients. It is believed that the time is appropriate for the writing of some papers discussing improvements in the use of plaster casts, which by and large throughout the country is justifiably the method of treatment by the general surgeon. It is recalled that one such article, that of Clarke,[245] appeared last year.]

A French article by Verne, Menegaux, Verne and Magnant [243] discusses the importance of selecting correct material and states that apparently there were only three steel alloys available in occupied Paris at the time of writing. A point that is brought out which seems reasonable is that hammering or forging should be avoided in the construction of plates and that they should have a high polish. The authors mention that care should be taken not to scratch the plates, but they are inconsistent in stipulating that the type of metal should be imprinted on the prosthesis.

Speed [244] has published a twenty page detailed article giving his mature ideas on the technic of open reduction and internal fixation. While no new points are mentioned, it is an excellent article by a past master and includes up to date and generally accepted ideas on this subject. It is a creditable discussion demonstrating the progress that has been made in the refinement of the technic for open reductions.

Plaster Technic.—Clarke [245] has written from England an excellent and refreshing résumé of plaster technic discussing the advantages of skin-tight plaster casts and stating that sores result more from friction than from pressure. He believes that the application of plaster casts directly to the skin is one of the major advances of recent years.

[ED. NOTE.—Much sound advice is given, but he does not mention the necessity of carrying the plaster to the end or very close to the end of an extremity to avoid a possible circulatory bottleneck. He calls attention to the value of 2 per cent borax in plaster water as an agent for delaying the time of setting of plaster without detrimental effect apparently to the strength of the final cast. He extols the Trueta "pattern-plasters" as time savers even in the application of such large casts as shoulder and hip spicas.]

A note of warning has been sounded by Archibald,[246] a Canadian, relative to the use of the sulfonamide compounds in war surgery. No chemotherapy, local

242. Venable, C. S.: Factors in Choice of Material for Bone Plates and Screws, Surg., Gynec. & Obst. **74**:541-545 (Feb., no. 2A) 1942.

243. Verne, J.; Menegaux, G.; Verne, J. M., and Magnant, J. B.: Tolerance for Certain Steels Used in Buried Prosthesis: Study of Osteosynthesis, Presse méd. **49**:452-455 (April 29) 1941.

244. Speed, K.: Technic of Application of Metal Plate to Oblique or Spiral Fracture of Long Bone, S. Clin. North America **22**:83-102 (Feb.) 1942.

245. Clarke, R.: War Surgery of Extremities: Plaster Technic, Brit. M. J. **1**:797-800 (June 27) 1942.

246. Archibald, E. W.: Casts New and Old in War Surgery (of Arms and Legs), Canad. M. A. J. **47**:93-102 (Aug.) 1942.

or otherwise, can be a substitute for early (within six hours) and thorough cleaning and débridement. When this has been done the closed plaster method is far superior to any method requiring splinting and frequent dressing.

Two articles have been published on facilitating the removal of casts, one by Roath [247] describing another electric cast cutter, which in view of previous experience with such instruments must prove its value by performance, and another by Price,[248] an Englishman, who suggests simply the pulling through of 24 gage piano wire under a cast by a petrolatum-smeared cotton tape laid on the skin prior to the application of the plaster. The cutting is completed according to the Bickford method of forcing the wire through the cast with a specially devised twister.

Galewski,[249] a Russian writing in England, advocates the use of a special silicate solution instead of plaster. Because of its lightness and toughness he believes it to be particularly appropriate for walking apparatus. To shorten its drying time, which is the drawback with all the silica preparations, he advocates local use of heat. It is feared that it is just another slowly drying material and therefore an impracticable substitute for the time-tested plaster, but more will doubtless be heard of it if it proves to be as valuable as is claimed.

The Council on Physical Therapy [250] has approved what is called a "cruricast bandage," a zinc gelatin paste being employed as the stiffening material. For office use it apparently is superior to a dressing prepared with soft paste of zinc oxide N. F. and has the same indications. It is claimed to be a "compressive and supportive dressing which is soft and resilient. This dressing is porous, to allow perspiration and evaporation, and is of sufficient strength to prevent expansion from pressure of body heat." As a dressing for application after the removal of a cast for those who feel the need of more support than is given by simple elastic woven bandages, it should be better than a dressing made with paste of zinc oxide and well worth trying.

Galland [251] describes a long-looked-for ischial seat brace for spica application. Such a device is needed particularly for the obese patient. It is hoped that one of the manufacturing houses will have this equipment on sale in the near future if they do not have it already. If it possesses only a few of the good qualities claimed, it will be an improvement on the conventional support that has been used over the years.

An almost complete elimination of the odor in the Orr treatment of osteomyelitis has been obtained by Wallis and Dilworth [252] with a dressing impregnated with an 18 per cent solution of lactose. This supplies an easily oxidizable carbohydrate for the putrefactive bacteria to work on, thus eliminating the production of the foul-smelling products of putrefying protein. As a result, casts can stay on longer, with more benefit to the patient. Another article on the elimination of odor in osteomyelitis was written by two English surgeons, Seddon and Florey,[253] who use cloth bags impregnated with carbon dust to put the offending part in. The

247. Roath, C. A.: Electric Cast Cutter, California & West. Med. **56**:78-79 (Feb.) 1942.
248. Price, C. W. R.: Removal of Plaster Casts: Modification of Bickford Method, Brit. M. J. **2**:772 (Nov. 29) 1941.
249. Galewski, S.: "Liquid Plaster" for Immobilization, Brit. M. J. **1**:225 (Feb. 14) 1942.
250. Cruricast Bandage Acceptable, report of the Council on Physical Therapy, J. A. M. A. **118**:456 (Feb. 7) 1942.
251. Galland, W. I.: Improved Ischial Seat Brace, J. Bone & Joint Surg. **24**:204-205 (Jan.) 1942.
252. Wallis, A. D., and Dilworth, M. J.: Odor in Orr Treatment: Prevention by Lactose, J. A. M. A. **120**:583-587 (Oct. 24) 1942.
253. Seddon, H. J., and Florey, H. W.: Filter Cloth for Controlling Smell from Plasters, Lancet **1**:755 (June 27) 1942.

material is called filter cloth, but nothing is mentioned as to where it may be obtained. In any event, the deodorizing quality of carbon has been employed and evidently found effective. It seems like a satisfactory alternative method to the use of lactose solution when redressing seems inadvisable.

New Splints and Apparatus.—A cleverly devised folding Thomas splint is described by Hosken [254] of England which, if it functions as efficiently as is claimed, is ideal for front line use. Its chief value lies in its portability and ease of application, for which real advantages strength has unquestionably been sacrificed. It would therefore be unsuitable for general civilian use.

Cohen [255] has devised a volar flexion splint which should be of value in preventing and correcting the distressing metacarpophalangeal hyperextension deformity. A principle not employed in other apparatus devised for the same purpose is used. It is apparently an efficient splint and should be investigated by those not satisfied with their present equipment.

Sponge rubber bandaged to the leg is advocated as an efficient means for traction by Barnard,[256] particularly when local physical therapy is desired or there is some other indication for frequent removal. It is felt that this is a means of obtaining traction well worth adding to one's armamentarium.

An instance of applying another carpenter's tool to surgical technic is suggested by Nicola,[257] who recommends a spirit level. Unfortunately, no information is given as to how to obtain the proper type of level, which apparently has to be specially made.

[Ed Note.—One wonders if the same excellent idea might be carried out with an inverted protractor incorporating a small hanging plumb bob.]

Criticism might be directed to an apparently efficient light fracture frame devised by Cleary [258] because a single pin is used in either fragment. It has many commendable features in addition to its avoidance of the cumbersomeness of the usual commercial equipment.

Ainsworth-Davis lays justifiable emphasis on the avoidance of metacarpophalangeal hyperextension [259] in another English paper in which he describes a steering wheel apparatus for grasping exercises for severely cicatrized hands. The apparatus is readily duplicated by a mechanic to whom old automobile parts are accessible. It would be a novel and useful device suitable to the physical therapy department of a large military hospital.

Several commendable new splint ideas have been reported of interest, particularly to the military surgeon, who has to improvise extensively, but do not contain sufficient new material to mention specifically and for lack of space have had to be left out. Among the best of these are Elliot's [260] "drop wrist" splint, Slocum's [261] shoulder abduction splint and Wilson's [262] modification of the banjo splint for fractures of the fingers and toes.

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254. Hosken, J. G. F.: Folding Thomas Splint, Brit. M. J. **1**:187 (Feb. 7) 1942.
255. Cohen, H. H.: Adjustable Volar-Flexion Splint, J. Bone & Joint Surg. **24**:189-192 (Jan.) 1942.
256. Barnard, H. I.: Rubber-Surface Skin Traction, J. Bone & Joint Surg. **24**:462-463 (April) 1942.
257. Nicola, T.: Use of Curved Spirit Level, Am. J. Surg. **57**:191-192 (July) 1942.
258. Cleary, E. W.: Light Fracture Frame: Uses and Construction, J. Bone & Joint Surg. **24**:694-698 (July) 1942.
259. Ainsworth-Davis, J. C.: Preservation of Function in Burnt Hand, Brit. M. J. **1**:724 (June 13) 1942.
260. Elliot, H.: Easily Made "Drop Wrist" Splint, Canad. M. A. J. **47**:363 (Oct.) 1942.
261. Slocum, D. B.: Simple Abduction Splint for Upper Extremity, Mil. Surgeon **91**: 26-29 (July) 1942.
262. Wilson, C. S.: Modification of Banjo Splint, Canad. M. A. J. **46**:585-586 (June) 1942.

A most useful and sure method of removing a ring from a swollen finger without cutting the ring is reported by Arbuckle.[263] A piece of string is passed under the ring. The one end is held on the proximal side of the ring, and the part distal to the ring is wound tightly around the well soaped finger. The proximal end of the string is then unwound against the proximal edge of the ring and forces the ring down over the finger.

[Ed. Note.—Try it. It's a good parlor trick anyhow, and soap is really not needed.]

Continued interest in the solution of the problem of discrepancy in length of the legs is evidenced by the appearance of seven new articles in 1942, all of them very good. The most important is the one by Gill and Abbott[264] on a practical method of predicting growth of the femur and the tibia in children. While most readers would feel that the method is too complicated for practical use, the article is undeniably of great importance, and it should be carefully read by all who contemplate this fascinating surgical problem. It is most important in the timing and location of operations designed to arrest growth. Many distressing experiences may be avoided if problems of this nature are worked out in accordance with the recommendations contained in this article. Due consideration is given to the age of bone maturation as recorded by Todd[265] in determining the probable age at which growth stops.

Howorth[266] discusses the leg-shortening operation, particularly in relation to the literature and history of the problem of inequality in length of the legs, and reports 17 operations, 11 of them being step-cut osteotomies with plate fixation. The article is thorough but does not mention the stimulation to growth of the shortened leg in a growing child by this procedure, a fact which must always be kept in mind.

[Ed. Note.—One of the editors (J. W. W.) has found in several instances in a series of over 80 cases that half of a 2 inch (5 cm.) correction in a growing child may be lost in the next year or two after such a procedure. He feels that it is an operation to be reserved only as a supplement to the operation for the arrest of growth when done before the age of bone maturation. The many time-consuming, traumatizing technics are more appropriate for the cabinet maker than for the surgeon. He recommends the simple overlap through and through screw fixation technic including all four strong, unweakened bone cortexes.]

Brockway and Fowler[267] report their experience with 105 leg-lengthening operations. Excellent results were achieved in 65 per cent of the cases, while in 22 per cent more they were considered good. Protection had to be continued on an average of nine months. Bony union was present in 57 per cent of cases in nine months and in 100 per cent in two and a half years.

[Ed. Note.—One of the editors (J. W. W.), who is an ardent leg shortener, feels that the dangers and complications were unjustifiably minimized in view of the experience of many other authors. He also feels that the authors have not given sufficient credit to the value of the growth arrest procedure and that sufficient

263. Arbuckle, M. F.: String Method of Removing Tight Ring from Swollen Finger, Mil. Surgeon **90**:184 (Feb.) 1942.

264. Gill, G. G., and Abbott, L. C.: Practical Method of Predicting Growth of Femur and Tibia in Child, Arch. Surg. **45**:286-315 (Aug.) 1942.

265. Todd, T. W.: Atlas of Skeletal Maturation, St. Louis, C. V. Mosby Company, 1937.

266. Howorth, M. B.: Leg-Shortening Operation for Equalizing Leg Length, Arch. Surg. **44**:543-555 (March) 1942.

267. Brockway, A., and Fowler, S. B.: Experience with One Hundred and Five Leg Lengthening Operations, Surg., Gynec. & Obst. **75**:252-256 (Aug.) 1942.

knowledge is available to perform this simple operation on growing children with as much certainty of success as can be expected with either the shortening or the lengthening procedure.]

Phalen and Chatterton [268] discuss rather in detail the problem of discrepancy in length of the legs and conclude that in a great majority of cases shortening is the method of choice. They believe that the admittedly more formidable lengthening should be reserved for those unusual cases in which loss of height is of serious consequence, for example when there is a possibility of future military service, an important point during these times.

In all studies of discrepancy in length of the legs, a satisfactory method of recording length is necessary. Merrill [269] describes a roentgenographic technic for the measurement of the actual size rather than the discrepancy in length of the long bones. The method is accurate but appears to be impracticable for clinical use and more suited to particular research problems, such as are encountered in experimental work on animals.

Irradiation as an agent in retarding bone growth is discussed by Kaplan,[270] who reports only 1 case, in which in twenty-eight months a discrepancy of 2½ inches (6.5 cm.) was reduced ¾ inch (2 cm.). It is apparent that much more research work must be done along this line before any safe and practical method can be recommended.

Flecker [271] has published a long article discussing growth of bone and the time of appearance and fusion of centers of ossification as observed by roentgenographic methods. He has found that several errors, of little practical importance to the orthopedic surgeon, however, are given in various tables. It is an excellent, thorough article of little practical interest, except to those orthopedic surgeons doing research work on bone growth. No serious discrepancies were noted in this paper when it was compared with the excellent chart by Camp and Cilley [272] of the Mayo Clinic, which appeared twelve years ago and which should hang beside every x-ray viewing box.

IX. TUBERCULOSIS OF BONES AND JOINTS

PREPARED BY ALAN DE FOREST SMITH, M.D., NEW YORK, ASSISTED BY THE STAFF OF THE NEW YORK ORTHOPAEDIC DISPENSARY AND HOSPITAL

Harris and Coulthard [273] have made an important study of 307 cases of tuberculosis of bones and joints treated in an institution in Toronto during the ten years from 1931 through 1940. They were able to follow 296 patients who were discharged from the hospital. The majority of these patients were adults. The diagnosis was proved bacteriologically in 70 per cent of the cases, and care was taken to exclude all in which there was any doubt of the cause.

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268. Phalen, G. S., and Chatterton, C. C.: Equalizing Lower Extremities: Clinical Consideration of Leg Lengthening Versus Leg Shortening, Surgery **12**:768-781 (Nov.) 1942.

269. Merrill, O. E.: Method for Measurement of Long Bones, Am. J. Roentgenol. **48**:405-406 (Sept.) 1942.

270. Kaplan, I. I.: Irradiation in Treatment of Limb Asymmetry, Arch. Pediat. **59**:559-564 (Sept.) 1942.

271. Flecker, H.: Time of Appearance and Fusion of Ossification Centers as Observed by Roentgenographic Methods, Am. J. Roentgenol. **47**:97-159 (Jan.) 1942.

272. Camp, J. D., and Cilley, E. I. L.: Diagrammatic Chart Showing Time of Appearance of Various Centers of Ossification and Period of Union, Am. J. Roentgenol. **26**:905 (Dec.) 1931.

273. Harris, R. I., and Coulthard, H. S.: Prognosis in Bone and Joint Tuberculosis: Analysis of Results of Treatment and Consideration of Factors Which Influence End Result, J. Bone & Joint Surg. **24**:382-395 (April) 1942.

All patients were treated by preliminary rest, which was followed by an operation to produce arthrodesis, except when it was contraindicated by advanced pulmonary lesions or other complications. The intent of the study was to discover the factors affecting the prognosis. It was concluded that active pulmonary tuberculosis, secondary infection of an abscess with sinuses and multiple tuberculous lesions, in that order, were the most important. Of the 296 patients, 28.6 per cent had multiple lesions elsewhere than in the lungs. Such lesions were chiefly in other bones. They retarded recovery and often necessitated several operations but did not greatly affect the mortality. Renal tuberculosis was found in 23 per cent. This also was not extremely serious as far as life was concerned. Secondary pyogenic infection in tuberculous abscesses, usually caused by improper treatment previous to admission, accounted for many fatalities and operative failures. Pulmonary tuberculosis was the gravest of all the complications. Whereas of those patients having no other than the bone lesion only 4 per cent died, of those having pulmonary tuberculosis from 20 to 80 per cent died, depending on the grade of pulmonary lesion. Forty per cent had pulmonary involvement. Eighty per cent of the patients with uncomplicated tuberculosis of the spine and 100 per cent of those with uncomplicated tuberculosis of the knee were cured and returned to work after arthrodesis. Of the 296 patients followed after discharge from the hospital, 28.6 per cent died. Ninety-six per cent of the deaths were caused either by some form of tuberculosis or by secondary infection of an abscess.

There was no evidence that the disease was disseminated by operation in any case. The type of infection was determined by culture, and not a single case of bovine tuberculosis was found.

[ED. NOTE.—This is a valuable study which confirms the conclusions which have been derived from other careful analyses of larger series of cases.]

Badgley and Hammond [274] report a review of 76 patients who had proved tuberculous arthritis of 77 hip joints and who had an arthrodesis as part of their treatment at the hospital of the University of Michigan Medical School between 1925 and 1935. The proof was obtained by pathologic and bacteriologic studies of tissue or material removed at operation or of pus from a cold abscess originating from the hip joint at some time during the patient's treatment. The age at the time of operation varied from 2 to 56 years. Almost two thirds of the patients (64 per cent) were between 6 and 20 years old.

The present plan of preoperative treatment consists of measures to build up the patients' general health and of immobilization to afford complete rest of the hip. These are continued until the general condition is good, until all other foci of tuberculosis are quiescent and until the patient has demonstrated his ability to combat the hip tuberculosis successfully. In the earlier years covered by this report, the arthrodesis was performed soon after the diagnosis was made, so that only 61 per cent of the patients in this series had preoperative care consistent with the aforementioned standards.

The types of operation were as follows: extra-articular, 53 per cent; intra-articular with extra-articular grafts, 30 per cent, and intra-articular, 14 per cent. The Hibbs operation constituted 60 per cent of the extra-articular procedures. Shock occurred in 4 cases and caused death in 2 (3 per cent). The average time for complete immobilization in plaster after operation was ten months, and with plaster followed by some other form of splinting, nineteen months. A second

274. Badgley, C. E., and Hammond, G.: Tuberculosis of Hip: Review of Seventy-Six Patients with Proved Tuberculous Arthritis of Seventy-Seven Hips Treated by Arthrodesis, J. Bone & Joint Surg. **24**:135-147 (Jan.) 1942.

arthrodesis was performed on 12 patients, or 16 per cent, because of failure of the first operation. In those in whom ankylosis of the hip developed, the average time required for clinical ankylosis was fifteen months and for bony ankylosis, as demonstrated by roentgenograms, sixteen months.

The end results are based on the history and the clinical and roentgenographic examinations. The average time from operation to final symptom examination (questionnaire) was seven years and five months; and between operation and final clinical and roentgenographic examination, five years. Both the subjective and the objective end results were considered, and the final classification of the patient represents a composite picture of the two. On this basis good results were obtained in 52 per cent, fair in 22 per cent and poor in 8 per cent. The total mortality was 18 per cent. The result was unknown in 5 patients. In all the 6 patients (8 per cent) who obtained a poor result, ankylosis was absent, and two thirds had secondary pyogenic infection of the hip with formation of sinuses and recurrent abscesses. Of the deaths, 8 per cent were due to unrelated diseases or unknown causes, 3 per cent to operative shock and 7 per cent to tuberculosis.

From careful studies of each case, certain factors were found which seemed to be important in relation to the outcome. Among them were the following:

1. Preoperative care of six months or longer was associated with much better results.

2. If the arthrodesis was not done before the age of 8 years or after the age of 30 the outlook was more favorable.

3. The presence of active pulmonary tuberculosis or of a sinus or cold abscess at the time of operation was associated with more unfavorable results.

4. If during the preoperative treatment the serial roentgenograms revealed improvement in appearance or progression in destructive changes followed by improvement, the prognosis was better.

5. The type of arthrodesis performed did not apparently influence the end result except in the case of intra-articular arthrodesis without bone grafts.

The authors propose from this study an optimum time for arthrodesis. There should be six months or more of preoperative treatment, which should be continued until (1) the patient is at least 8 years old; (2) any abscess or sinus about the joint has disappeared; (3) there is no evidence of active pulmonary tuberculosis, and (4) there is roentgenographic evidence of improvement in the lesions.

[Ed. Note.—The results of the series parallel quite clearly those in patients treated at the New York Orthopaedic Hospital, where only 66 per cent of the primary operations produced a bony fusion. By doing second and third operations on the remainder the number of successful results was raised to nearly 90 per cent. No single operative technic is applicable to all cases. The procedure must be adapted to the patient.]

Roth [275] presents a follow-up study of patients on whom an arthrodesis of the hip joint was performed for tuberculosis. One hundred and eleven patients with clinical tuberculosis of the hip joint were seen at the Hospital for Joint Diseases in New York city from 1928 to 1940. Fifty of these had an arthrodesis performed, and of these 4 were discarded from the study because of inadequate records and 1 because of doubt of the diagnosis. For 27, or 60 per cent, of the remaining 45 hips the diagnosis was proved by bacteriologic or histologic examination. Five

275. Roth, F. B.: Results Following Arthrodesing Operations for Tuberculosis of Hip, Bull. Hosp. Joint Dis. **3**:153-162 (Oct.) 1942.

of the patients had more than one clinically apparent focus of tuberculosis, 1 in the lungs, 1 in the opposite hip and 3 in the lumbar portion of the spine.

Fifty-seven arthrodeses were done on the 45 patients. Ten of these were secondary and 2 were tertiary procedures. An extra-articular arthrodesis was performed in 93 per cent of the cases and a combined extra-articular and intra-articular operation was done in 5 per cent. In 1 patient, tibial grafts were driven through the neck of the femur into the acetabulum.

A preoperative program of conservative care of from six to twelve months was carried out for the majority of children but only for a minority of the adults. Such a program is considered worth while for children, as it usually leads to an improvement in the local and the general condition of the patient.

Firm bony union was judged to have occurred when there was no longer any doubt as to its presence. Nineteen, or 61 per cent, of the 31 hips fused after one operation. This figure was raised to 24, or 77 per cent, by secondary arthrodeses and to 26, or 84 per cent, by tertiary arthrodeses.

Poorer results were obtained in those patients that had local abscess formation at the time of operation. The average times for fusion were nineteen months for the patients who had had a local sinus within the year before operation, forty-two months for those with local abscesses and sixteen months for those without complications. About three quarters of the operations were done before the patients were 17 years old. No patient operated on before the age of 6 obtained a fusion. If the 5 patients that had an additional focus of disease are excluded, postoperative sinuses developed within three months after 23, or 44 per cent, of 52 operations. All but 9 of the 23 obtained complete healing of the skin during observation. There was no immediate operative mortality in this group of 40 patients, but several deaths occurred later. One patient died two months after arthrodesis from tuberculous meningitis and miliary tuberculosis. Two died after five months and thirteen years respectively from secondary infection of the hip subsequent to a postoperative sinus, and 1 died after six and one-half years from infection of the genitourinary tract subsequent to a secondary infection of the hip originating in a postoperative sinus.

[ED. NOTE.—Although arthrodesis is more difficult in the tuberculous hip of a child under 6 years of age, it has been done successfully in many young children. Because of the disastrous consequences of other methods of treatment in such patients we believe that the operation should be performed whenever the patient's condition permits, regardless of age.]

After commenting generally on tuberculous joints and mentioning the methods of iliofemoral arthrodeses of Albee, Hibbs and Wilson and the ischiofemoral technics of Trumble and Brittain, Coolican [276] describes his method of placing a tibial bone graft between the adductor muscles from the pubis to the femur. Arthrodesis by a bone graft below the joint is considered more desirable, because a graft in such a position is better able to oppose the greater amount of strain that results from the long axis of the femur and the flexor-adductor muscles. In addition, the graft lies in a healthy bed remote from the seat of infection.

With the patient lying on an abduction frame with a hinged leg bar, a 6 inch (15 cm.) incision is made from the pubic tubercle down the line of the adductor longus muscle. The deep fascia is divided over the interval between this muscle and the gracilis. The line of cleavage is opened between the adductor longus in

276. Coolican, J. H.: Bone Grafting in Tuberculous Hips, Irish J. M. Sc., April 1942, pp. 128-132.

front and the adductor brevis and the adductus magnus behind. The adductor longus is retracted, exposing at the bottom of the wound the deep femoral artery with its first perforating branch and the inner side of the femur. The profunda vessels are displaced, and an oval opening is drilled into the femur after subperiosteal exposure about 2 inches (5 cm.) below the lesser trochanter. The adductor longus tendon is partially or completely divided at its origin, and the body of the pubis is exposed beneath the pubic tubercle. A pit of suitable size is drilled in the bone, and a graft is then cut from the tibia on the affected side. This is securely fitted into place between the femur and the body of the pubis, and the wound is closed without drainage. A plaster spica including the frame is applied and left undisturbed for three months, except for being split and reenforced after eight or ten days for removal of the stitches.

Five case reports are briefly given. In all of these roentgenograms showed that the grafts were united at twelve, thirteen, eight, four and two months after operation.

[ED. NOTE.—Ischiofemoral or pubofemoral arthrodesis is of value in tuberculous hips in which there is an extensive destruction of the ilium as well as of the femoral head and neck. In addition to the procedures mentioned in this paper, that of Bosworth should be noted. All of these operations are technically difficult.]

A new technic for arthrodesis of the elbow for tuberculosis is presented by Nickerson,[277] and 3 case histories are reported. The procedure is similar to that of Hallock, in that the graft is taken from the olecranon and the triceps muscle is left attached. Nickerson's method differs in that a U-shaped wedge of bone is taken from the olecranon, so as to leave the medial and lateral portions of the olecranon intact. The proximal end of the graft is inserted into the humerus and the distal end wedged into the "fish" mouth of the olecranon. The triceps tendon is then plicated on itself. Three cases are reported in which fusion was obtained after one operation.

Wassersug [278] reviews 46 cases of tuberculosis of the ankle and 42 of the foot in which the patients were treated at the Lakeville State Sanatorium in Massachusetts. Seventeen of the 46 patients with involvement of the ankle died. Eleven of them had some other tuberculous focus. The diagnosis was proved in 40 cases. Three patients who had an arthrodesis performed died. Amputation was necessary in 11 patients who were treated conservatively. In the group with tuberculosis of the foot, 3 died. Two arthrodeses were performed, and there were 7 amputations.

[ED. NOTE.—This is an unusually high percentage of deaths and amputations in a series of patients with involvement of the foot and ankle. Delay in diagnosis and treatment before the patients were received and serious complicating lesions may explain these results. Certainly experience has shown that when an early diagnosis is made and arthrodesis is done cure results in a great majority of cases.]

Cleveland and Bosworth [279] give an illuminating report of a study of pathologic material from cases of tuberculosis of the spine from their service at Sea View Hospital, New York.

They found no evidence that tuberculosis begins in the intervertebral disks, but found that it practically always has its inception in the vertebral bodies.

277. Nickerson, S. H.: Modified Approach in Surgery for Tuberculosis of Elbow in Adult, Am. J. Surg. **56**:483-487 (May) 1942.

278. Wassersug, J. D.: Tuberculosis of Foot and Ankle in Adults and Children, New England J. Med. **227**:436-439 (Sept. 17) 1942.

279. Cleveland, M., and Bosworth, D. M.: Pathology of Tuberculosis of Spine, J. Bone & Joint Surg. **24**:527-546 (July) 1942.

In the latter, two processes were found, the first a caseating, destructive lesion, such as usually has been described, and the second a sclerosis of bone associated with necrosis. The latter either had the pattern of an infarct from the occlusion of an artery or was peripheral. The authors conclude that the sclerosis is caused by interruption of the blood supply to the vertebral body by stripping up of the periosteum by an abscess. This may occur over a wide area and may spread for some distance from the original focus. Examination of the spines at autopsy revealed many lesions which were not demonstrated by roentgenograms either of the spine as seen before the patients died or of the specimens taken afterward.

[ED. NOTE.—The frequency of a sclerosing necrosis of bone from deprivation of blood supply in spinal tuberculosis has not been generally appreciated. The finding that the disease does not begin in the intervertebral disk, however, has been generally accepted. One of the earliest roentgenologic findings is thinning of the intervertebral disk, but this is not due to early invasion by disease. It has been the experience of one editor (A. D. S.) also that many tuberculous lesions of the vertebral bodies cannot be detected by the usual roentgenographic examination. Several of these obscure lesions have been successfully demonstrated by means of the laminagraph, and it is advised that this means be employed in doubtful cases when it is available.]

Auerbach [280] reports that at Sea View Hospital, in New York, the department of pathology performed in eight and one-half years 95 autopsies for tuberculosis of the thoracic vertebrae and the ribs. Fifteen of these revealed abscesses that had ruptured into the lung. Three abscesses had ruptured into the pleural cavity.

The cause of perforation is enlargement of a paravertebral or costal abscess by increasing amounts of liquefied caseous material. A perifocal reaction occurs in the overlying pleura, producing thickening and firm adhesion to the endothoracic tissue. All fascial planes are thus obliterated, and no further extension of the abscess can occur. As it continues to enlarge, it must progress into the parenchyma of the lung and rupture into the bronchi.

The extension is entirely different when there is perforation into the pleural cavity. Here a tuberculous pleuritis must be present before the perforation occurs, with the tuberculous exudate within the pleural space, keeping the visceral and parietal layers separated.

The symptoms of onset are sudden cough and copious expectoration. The sputum suddenly begins to contain tubercle bacilli. Dense pneumonic shadows appear in previously clear lungs. There is an atypical location of the pulmonary tuberculosis, because it is adjacent to the site of the lesion in the bone. Cold abscesses appear generally in the lower lobe.

A clinical report is made by Monfort and Solomon [281] of a 16 month old Negro boy who after trauma to the head had a lesion of the skull. The skull and the left humerus roentgenographically exhibited punched-out, circumscribed bone defects described as osteitis tuberculosa multiplex cystoides. Biopsy specimens from the lesions in the skull and in the humerus were histologically characteristic of tuberculosis. Additional clinical diagnoses were mediastinal lymphoglandular tuberculosis, mastoiditis and tuberculosis of the spine.

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280. Auerbach, O.: Rupture of Cold Abscesses into Lungs and Pleurae, Clinics **1**:600-614 (Oct.) 1942.

281. Monfort, J. A., and Solomon, N. H.: Osteitis Tuberculosa Multiplex Cystoides in Children, Am. J. Dis. Child. **63**:346-353 (Feb.) 1942.

Meng and Wu [282] describe 40 cases of adolescents with tuberculosis of the cranium secondary to tuberculosis of the lungs or joints, cold abscesses or sinuses.

[ED. NOTE.—The great prevalence of tuberculosis in China results in the occurrence of many lesions which are rare in this country. Reports of such lesions are interesting and of some value in throwing light on the occasional case seen here.]

A case is reported by Sweet and Abramson [283] of a 3 year old Negro child with bacteriologically proved tuberculous lesions of the left radius, right ulna and left fifth metacarpal bone associated with swelling of the soft parts and formation of sinuses. Roentgenograms of these long bones exhibited periostitis, expansion of shafts and cystlike areas of resorption of medulla and cortex which the authors report as multiple cystic tuberculosis. Criteria are outlined for differentiating this condition from Jüngling's disease.

De Gara [284] reports on 195 patients with extrapulmonary tuberculosis examined from 1934 to 1939 in northern Italy. Tubercle bacilli of the bovine type were found in 18, or 9.2 per cent. Of these patients 174 had tuberculous lesions of bones and joints; in 13 (7.4 per cent) the lesions were caused by bacilli of the bovine type. The remaining 21 patients had lesions of the cervical lymph nodes; in 5 of these (23.8 per cent) the lesions were due to organisms of the bovine type.

Bovine tuberculosis was observed in 40 per cent of the affected children less than 5 years of age, in 16.6 per cent of those between the ages of 5 and 15 years, and in 6.4 per cent of the persons older than 15 years.

The importance of infected raw milk or of prolonged contact with infected cattle in the causation of infection with bovine tubercle bacilli is described. Included is a table compiled from the literature on the incidence of the bovine type of tuberculosis of bones and joints in various European countries.

[ED. NOTE.—The marked decrease in the incidence of tuberculosis of the bones and joints with the almost complete elimination of tuberculosis of the cervical lymph nodes coincident with the pasteurization of milk and testing of cattle in the greater part of the United States is further proof of the importance of bovine infection in the causation of osseous lesions in children.]

Biopsy study of regional lymph nodes was made by Webster [285] in 15 instances of tuberculous joints. The histologic and cultural methods employed gave consistent results, except in 1 case in which the result of culture was negative. Only the human type of Mycobacterium tuberculosis was reported as being found.

Tuberculous lymphadenitis was demonstrated in the inguinal lymphatic nodes in 6 of 7 patients, all but 1 of whom were children, suffering from tuberculosis of the knee joint; in nodes of the same group in 2 of 6 children suspected of tuberculosis of the hip joint; in an inguinal node also of 1 adult patient exhibiting advanced tuberculosis of the ankle joint and in an axillary node of a child with tuberculosis of the wrist joint. Lymphatic drainage of joints is discussed and reasons are suggested against the acceptance of the finding of tuberculosis in lymphatic nodes of the superficial inguinal group as significant of tuberculous disease of the hip joint. In 15 patients with nontuberculous arthritis, biopsy specimens of the regional lymphatic nodes showed no evidence of tuberculosis.

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282. Meng, C. M., and Wu, Y. K.: Tuberculosis of Flat Bones of Vault of Skull: Study of Forty Cases, J. Bone & Joint Surg. **24**:341-353 (April) 1942.

283. Sweet, L. K., and Abramson, D. J.: Multiple Cystic Tuberculosis of Long Bones, J. Pediat. **19**:826-832 (Dec.) 1941.

284. de Gara, P. F.: Bovine Tuberculosis: Its Incidence in Bone, Joint and Cervical Lymph Node Lesions in Italy, Am. Rev. Tuberc. **45**:576-585 (May) 1942.

285. Webster, R.: Studies in Tuberculosis: Biopsy Study of Lymphatic Glands in Diagnosis of Tuberculous Disease of Joints, M. J. Australia **1**:160-166 (Feb. 7) 1942.

Howard, Johnston and Mitchell [286] measured the sensitivity to tuberculin in children by using dilutions of old tuberculin and determining thresholds of reaction in 19 patients with tuberculosis of bone. All presented evidence of primary pulmonary infection, the process being active in most cases and healed in several. Nine showed multiple involvement of bones or other tuberculous complications. In 4 children 2 years old the initial threshold reactions at the start of osseous involvement were elicited by 0.1 to 0.01 mg. of old tuberculin. These amounts subsequently fell to 0.0001 to 0.00000001 mg. and then rose again to 0.01 and 0.001 mg. with the healing of the process three to seven years later. A second group of 7 children who did not appear for treatment until after bones were involved had the same rise and fall pattern of allergy. A group of 5 children showed a high plateau of sensitivity for from three to six years, associated with poor ability to heal. There was 1 death from constantly spreading tuberculous infection. On the basis of this series, which the authors admit is small, it is concluded that a rise to a high level of sensitivity with a subsequent fall is characteristic of the evolution of the healing process in osseous tuberculosis, and that sustained high levels of allergy have characterized lesions which have shown a failure to heal.

X. INFECTIONS OF BONES AND JOINTS EXCLUSIVE OF TUBERCULOSIS

PREPARED BY PAUL C. COLONNA, M.D., PHILADELPHIA
ASSISTED BY E. B. DUNLOP, M.D., DAVID J. KING, M.D., AND THOMAS GUCKER, III, M.D.

General Considerations.—Mahorner and Crain [287] review 178 cases of acute hematogenous osteomyelitis: Sixty-six patients were treated in the years 1937 to 1940, with a mortality of 6.6 per cent, and 112 in the years 1930 to 1936, with a mortality of 24 per cent. Treatment was carried out as follows:

1. Hydration and replacement of electrolytes were achieved by administration of dextrose and isotonic solution of sodium chloride.

2. Protein replacement with repeated transfusions.

3. Oral chemotherapy with daily doses of 0.2 Gm. of sulfathiazole per kilogram of body weight or intravenous chemotherapy with amounts of a 5 per cent solution sufficient to provide 0.06 Gm. per kilogram of the drug in twenty-four hours had definite value. The rationality of the type of chemotherapy employed was verified by cultures.

4. Immunotherapy with staphylococcus antitoxin and staphylococcus toxoid is a recent development.

5. After the patient had been prepared by the foregoing measures and the disease had endured long enough for pus to form, incision and drainage or osteotomy was done and petrolatum gauze packing inserted. Early emergency operation may convert periostitis into osteomyelitis. Ligation of veins is indicated if cultures of the blood remain positive and sequestrectomy should be done if there is continuation of drainage and inflammatory reaction with or without roentgen evidence.

6. Immobilization by means of traction or a plaster cast is important and may in some cases be solely responsible for a drop in temperature when other methods are ineffectual.

286. Howard, P. J.; Johnston, J. A., and Mitchell, C. L.: Tuberculin Sensitivity in Children with Bone Tuberculosis, Am. Rev. Tuberc. **46**:532-545 (Nov.) 1942.

287. Mahorner, H., and Crain, A. P., Jr.: Acute Hematogenous Osteomyelitis, Ann. Surg. **115**:790-815 (May) 1942.

Follow-up of 42 of the 66 patients in the 1937 to 1940 series revealed that in 20 (47.6 per cent) the infection had healed in an average time of seventeen months. Fourteen had been subjected to osteotomy and 7 to incision and drainage, and 1 had not been operated on. Thirty-four patients wore plaster encasements for an average of eleven months. Of the 13 patients who were given sulfathiazole, 8 had staphylococcus bacteremia and 4 wounds from which staphylococci could be cultured. Six patients were given staphylococcus antitoxin. The authors conclude that ligation of veins is a safe adjunct to treatment, though its effectiveness has not yet been proved.

This article emphasizes the fact that since osteomyelitis is a vascular or intravascular disease venous ligation constitutes reasonable treatment. Recent studies on the pathogenesis of osteomyelitis suggest that it begins under the periosteum or in the cortex of the bone and causes osseous cellulitis.

[ED. NOTE.—The authors are optimistic to call the infection healed after a short follow-up period.]

Buchman [288] discusses three forms of osteomyelitis:

1. Acute osteomyelitis: In explaining its pathogenesis he mentions a theory of localization based on the fact that phagocytosis is less in the metaphysis than in the diaphysis. He stresses the importance of the invasiveness of bacteria, rather than their toxigenicity, in the production of osteomyelitis and also speaks of a "spreading factor" described by Duran-Reynals which increases the permeability of the tissues to bacteria. He suggests variations in treatment for each of four types of acute osteomyelitis: (1) fulminating, (2) severe acute, (3) ordinary acute and (4) mild. General treatment should include rest, blood transfusions and administration of fluids. Immunotransfusions to overcome bacteremia and antitoxins to combat toxemia are also helpful. Local treatment consists of prompt, efficient and conservative surgical drainage of metaphysis followed by packing with petrolatum gauze and immobilization in a circular plaster of Paris bandage for four to six weeks. For infants under 2 years and for the fulminating and severe acute types of the disease, he advises primary consideration of systemic invasiveness and toxemia, operative intervention being delayed until the former is under control and definite evidence of a local osseous lesion is present.

2. Postacute osteomyelitis: Here there is a slow downhill course with persistent draining sinuses, pathologic fractures and deformities. General treatment includes a diet of high caloric value and rich in vitamins. Secondary anemia is treated with hematinics, liver extracts and transfusions. Local treatment consists of thorough drainage and the use of plaster supports.

3. Chronic osteomyelitis: This is characterized by local lesions intermittently healing and becoming reactivated. It is treated by excision of diseased tissue as radically as possible, saucerized wound being lined with petrolatum gauze and the cavity packed with dry gauze. A huge compression bandage is then applied. Plaster is used only when a pathologic fracture is anticipated. A week to ten days later the packing is removed, sterile maggots are implanted and the wound is covered with a single layer of fine-meshed cheesecloth held in place by liquid adhesive. Maggots are replaced as soon as they die, and renewal is continued as long as necessary. The author believes that allantoin, urea and maggot substitutes are much less effective because they "lack the stimulus to rapid formation of granulations resulting from the subminimal physical irritation incidental to the continuous crawling about of the maggots."

288. Buchman, J.: Osteomyelitis, in Litchfield, H. R., and Dembo, L. H.: Therapeutics of Infancy and Childhood, Philadelphia, F. A. Davis Company, 1942, vol. 4, p. 3732.

The author raises the question of how to treat lesions which appear clinically to be new but which roentgenograms reveal to be chronic. He concludes that in the acute phase sulfonamide compounds are beneficial only to overcome bacteremia and do not significantly influence either primary or secondary foci and that in the chronic stage they are even less valuable. He mentions Dickson, Diveley and Kiene's method of preoperative and postoperative oral administration of sulfathiazole combined with topical application of the drug to the saucerized wound, which is closed without drainage. He feels, however, that this method is still in the experimental stage.

[Ed. Note.—There is insufficient emphasis on immobilization in plaster, both in the acute and in the chronic stage. The author is somewhat too pessimistic about therapy with sulfonamide compounds.]

Brailsford,[289] in discussing chronic abscesses of bone, states that the clinical features are attacks of pain in the affected extremity, which may be mild or severe and are initiated by jarring. There may be no local signs of inflammation and no changes in the subcutaneous tissue, and the patient may be afebrile. Local swelling may be noted if the involved part of the bone is near the skin. Trauma appears to be a causative influence. The lesions seem to be more frequent between the ages of 10 and 20. Clinically it may have to be differentiated from a neurologic condition (herniated intravertebral disk).

The roentgenogram generally shows a spindle-shaped accretion of new periosteal bone with a central translucent area on a plane with the original periosteum. The new bone at first is less dense than the normal cortex, and the latter becomes absorbed into new bone. There is no clear demarcation at the boundary between new and normal bone.

The treatment consists of a localized resection of the cortex, including the central focus. On section the tissue appears like osteoid osteoma, which in its early stages shows a large amount of osteoid tissue, later becoming calcified. Hence from the roentgen appearance it may be mislabeled chronic sclerosing, nonsuppurative osteomyelitis, intracortical abscess, syphilitic osteoperiostitis, sclerosing osteogenic sarcoma or osteochondritis dissecans.

[Ed. Note.—The author has made no mention of antecedent or coincidental cutaneous infections, and in 4 cases diagnosis was not confirmed by operation, since none was performed.]

Maxfield and Mitchell[290] report 5 cases of acute osteomyelitis in the adult and stress the point that it has so many characteristic clinical manifestations that it should be considered a separate clinical entity. Staphylococcus aureus is usually the organism found, but in 1 of their cases, which was fatal, hemolytic streptococci were noted. In 2 cases the disease was localized in the femoral shaft and was accompanied by pathologic fractures. These authors stress the fact that the onset of the disease is a matter of weeks or even months, that the pain is vague and that the pathologic changes are most apt to center near the middle of the diaphysis. An early manifestation is a light periosteal reaction, and they believe that there are two distinct pathologic types, one characterized by primary periosteal involvement with secondary invasion of the medullary shaft and the other by a low grade infection of the central area with secondary spread to the periosteum. In the latter type, with one or more central areas of rarefaction, the condition may be interpreted

289. Brailsford, J. F.: Chronic Sub-Periosteal Abscess, Brit. J. Radiol. **15**:313-317 (Nov.) 1942.

290. Maxfield, E., and Mitchell, C.: Acute Hematogenous Osteomyelitis in Adult, J. Bone & Joint Surg. **24**:647-652 (July) 1942.

as an abscess of bone if only a casual examination is made, but the authors point out that the abscess does not show a light periosteal reaction but there is an area of sclerosis around its margin. In addition it differs from the adult form of acute osteomyelitis in that it is characteristically near the epiphysis rather than in the center of the diaphysis. The treatment consists of adequate drainage.

[ED. NOTE.—The diagnosis of this disease may be extremely difficult, particularly when the infection is in the central area primarily. For this reason early exploration may prevent the process from going on to pathologic fracture. Wide saucerization followed by the Orr method of treatment is advocated.]

Meyerding and Clegg,[291] after reviewing the pathology and clinical picture of osteomyelitis, stress the value of the use of sulfanilamide and sulfathiazole. They point out that the marked similarity of Ewing's tumor and osteomyelitis, as revealed by the symptoms and roentgenographic findings, cannot be overemphasized. In discussing acute osteomyelitis they state, surprisingly: "Although most authors still advocate immediate incision and drainage and the instillation of petrolatum packs (Orr's method of treatment) or the use of dakinization, some believe that incision of periosteum and soft tissue abscess is preferable." The authors feel that the sulfonamide compounds are especially effective in cases in which septicemia is a complicating factor and recommend sufficient amounts of these drugs to maintain a concentration of 10 mg. per hundred cubic centimeters of blood. The local administration of 10 to 15 Gm. of the powdered drug is indicated as an adjunct in the treatment of open wounds. They contend that the drug should be injected into sinuses or cavities when mixed with cod liver oil—5 Gm. of either drug with 30 cc. of oil. Although they realize that there may be certain individual hypersensitivities to chemotherapy, they have not encountered any serious damage from the use of either of these drugs.

A report is then made of 8 illustrative cases showing the occasional difficulty of differentiating osteomyelitis from Ewing's tumor and demonstrating the chronic persistence of osteomyelitis for twenty-six years. The authors mention the possibility that malignant disease may develop in infections associated with long drainage. Several other cases illustrative of the value of adequate chemotherapy are reported. The authors believe that the drug should be taken both orally and locally in all cases of osteomyelitis and septicemia. When the drug is taken before localization of the disease in the bones adequate chemotherapy may prevent osteomyelitis and its complications. The authors feel that when large abscesses have formed adequate surgical drainage of the infected region should still be done.

[ED. NOTE.—The bacteriostatic action of the sulfonamide compounds plus adequate surgical treatment in osteomyelitis, whether of streptococcic or staphylococcic origin, has paved the way for the development of many other drugs. The authors' statement regarding the widespread use of the Orr treatment in acute osteomyelitis is not accepted by the editors. The recent report on penicillin would seem to indicate that in this drug one has an even more potent substance for combating the Staphylococcus aureus.]

In an article designed to evaluate the present methods of treatment of chronic osteomyelitis (namely, treatment by the Carrel-Dakin and the Orr method, treatment with "bipp" and treatment with maggots), Buchman [292] reviews briefly the history of the treatment of this condition, its pathology, the "basic surgical attack"

291. Meyerding, H. W., and Clegg, R. S.: Modern Treatment of Osteomyelitis, Am. J. Surg. **57**:56-64 (July) 1942.

292. Buchman, J.: Treatment of Chronic Osteomyelitis, S. Clin. North America **22**:581-595 (April) 1942.

(tourniquet control, a liberal incision, stripping of the periosteum within the limits of incision, saucerization from normal bone above to normal bone below, removal of all visible foci and overhanging shelves, thorough cleansing with hot isotonic solution of sodium chloride to remove debris and to control oozing, and immobilization of the part), and the problem of closure of the wound. (The author stresses the importance of the time factor involved in the formation of healthy granulation tissue, which should proliferate with sufficient rapidity to fill the entire cavity before the blood supply is damaged by the forming fibrous tissue.)

With the foregoing considerations in mind, Buchman established the following criteria for successful treatment:

1. Thorough surgical removal of all diseased and scarred tissue, and removal of all foreign bodies.

2. Efficient removal of wound discharges.

3. Efficient and harmless disinfection of the wound.

4. Even and rapid filling of the wound with healthy granulation tissue before circulation has become impaired.

The Carrel-Dakin method fulfils only the first two of the above prerequisites; the Orr method fulfils the first, second and third, but the author recognizes it as effective under war conditions; treatment with "bipp" (bismuth subnitrate, iodoform and petrolatum paste) is similar in effectiveness to the Orr method; treatment with maggots fulfils all of the criteria listed by the author, who strongly favors this method for handling selected cases.

The importance of not overlooking the systemic aspects of osteomyelitis is brought out. The diet should be of high caloric value and rich in vitamins, and proper hygienic care should be insisted on. In the presence of secondary anemia, hematinics, liver therapy and transfusions may be indicated.

[ED. NOTE.—This is an excellent résumé of the subject, though the editors feel that the disadvantages of the use of maggots have not been sufficiently stressed in this article.]

Traumatic Wounds.—Livingston [293] reports a study of 22,954 fractures of long bones received in battle. Eighty per cent of these battle fractures were compound, and about one half of the compound fractures required over five years to become stationary. He believes that mobile hospitals should be equipped so that a major surgical operation can be performed within seventy-two hours after injury. In 1930 there were 10,000 cases of old and recent osteomyelitis in the Veterans Administration.

The author reached the following conclusions:

1. Compound fractures should have early anatomic alinement by open or closed manipulation and should be maintained by internal or external fixation. Hardware can be used at the time of débridement and infection does not contraindicate its use.

2. Thorough, careful débridement is advisable.

3. Antitetanus and anti-gas-gangrene serums should be given prophylactically in all cases and should be repeated before delayed operation is attempted.

4. Shock should be treated by intravenously injected serum or plasma.

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293. Livingston, S. K.: Results in Compound Fractures with Osteomyelitis as Experienced by Veterans Administration over Past Twenty Years, Surg., Gynec. & Obst. **74**:546-548 (Feb., no. 2 A) 1942.

5. Both oral and local treatment with sulfonamide compounds are recommended.

6. Sequestrectomy in chronic osteomyelitis should be thorough and should include areas of osteosclerosis. Progressing molecular necrosis requires either amputation or wide excision to areas obtaining their blood supply from the collateral circulation.

7. Symes and Gritti-Stokes amputations are those of election. Amputation at the calf should usually be avoided.

8. Treatment with maggots and treatment by the Orr method are both effective for osteomyelitis.

9. Local irrigating solutions, antiseptics and pastes are not effective in the treatment of osteomyelitis.

Caldwell [294] divides traumatic lesions into abrasions and incised, punctured, lacerated, contused and gunshot wounds and states that the organisms usually found are the staphylococcus, the streptococcus and the anaerobes producing tetanus and gas gangrene. He stresses the fact that the only effective treatment of post-traumatic infections is preventive. Stressing the benefit of the sulfonamide compounds both orally and intravenously, he cites experimental work showing that immediate implantation of the sulfonamide derivatives at the time of the accident followed by an adequate surgical procedure and reimplantation of the drug locally is most effective in preventing all infections.

The ideal plan he outlines would consist of immediate implantation in the wound of 5 to 20 Gm. of sulfathiazole, use of transportation splints and appropriate shock treatment, thorough débridement within six hours of injury, with reimplantation of sulfathiazole, primary closure of the wound, unless more than six hours has elapsed, and intravenous or oral administration of sulfathiazole for five to seven days postoperatively. Tetanus antitoxin and combined tetanus and polyvalent gas gangrene antitoxin should be administered routinely to all patients with incised, lacerated or punctured wounds.

[Ed. Note.—This is an excellent summary of the treatment of infection developing after trauma to the extremities.]

Types of Osteomyelitis.—To illustrate the confusion in the diagnosis of osseous syphilis, Alexander and Schoch [295] present 2 cases in which the clinical manifestations were unusual and difficult of explanation. Because of the negative serologic report, confusion arose, and in 1 case diagnosis was greatly delayed, while in the other tuberculosis was considered the most likely diagnosis. In each of these cases the patient responded dramatically to antisyphilitic therapy. The authors make the pertinent comment that if syphilis is even suspected a trial of antisyphilitic treatment is advisable before more radical measures are attempted.

[Ed. Note.—One is constantly being reminded of the multiplicity of lesions attributable to the ubiquitous Treponema pallidum.]

Rosenberg, Dockerty and Meyerding [296] state that of 514 cases of coccidioidal granuloma reported up to April 1941, with 249 deaths, approximately 90 per cent

294. Caldwell, G. A.: War Surgery and Traumatic Lesions: Post-Traumatic Infections of Extremities, Am. J. Surg. **56**:64-69 (April) 1942.

295. Alexander, L. J., and Schoch, A. G.: Osseous Syphilis: Confusion in Diagnosis; Report of Two Cases of Osteomyelitis of Late Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **26**:397-406 (July) 1942.

296. Rosenberg, F.; Dockerty, M. B., and Meyerding, H. W.: Coccidioidal Arthritis: Report of Case in Which Ankles Were Involved and Condition Was Unaffected by Sulfanilamide and Roentgen Therapy, Arch. Int. Med. **69**:238-250 (Feb.) 1942; correction, ibid. **69**: 717 (April) 1942.

were in patients observed in California and 66 per cent have been reported from the central and southern sections of the state.

Until recently, the fungus Coccidioides immitis was thought to cause only one type of disease, a chronic granulomatous infection with clinical and pathologic features similar to those of tuberculosis and known to affect the skin, the lymph nodes, the abdominal and thoracic viscera, the meninges and the bones and joints. Endemic in the Sacramento–San Joaquin Valley area for fifty years had been a disease known locally as "valley fever," "desert fever," "desert rheumatism," "San Joaquin Valley fever" or "the bumps" and characterized by acute onset of malaise, general aches and pains, "toxic erythema," sore throat with fever, and occasionally conjunctivitis and signs of bronchopneumonia. Eight to fifteen days after onset, when improvement of the aforementioned symptoms is noticed, lesions typical of erythema nodosum appear, mainly on the skin. Roentgenograms of the chest at that stage of the disease disclose the presence of opaque areas suggestive of tuberculosis. Until 1936 the cause of this disease remained unknown. At that time Dickson and Smith found that the fungus C. immitis could be obtained from sputum of patients and that positive subcutaneous injection of test doses of a broth filtrate (coccidioidin) could be made.

There are two phases in the life cycle of C. immitis. During the vegetative phase, the fungus lives in soil and vegetation, and during the parasitic phase it inhabits the body of the infected host. The modes of entry are inhalation, direct contact with abrasions of the skin and "inoculation infection."

Involvement of joints occurs both in the acute benign phase and the chronic granulomatous phase of coccidioidal infection. Acute arthritis develops in about one third of the patients with "valley fever," usually appearing simultaneously with erythema nodosum and always clearing without residual damage or deformity. Treatment consists of rest in bed, symptomatic relief by administration of salicylates, etc.

Lesions of bones and joints are fairly common in the chronic granulomatous stage of the disease. Arthritis, often multiple, was present in 79 of 256 cases reported in 1931. Early the joints are swollen and red; later fluctuation may appear. Nodular lesions may develop in skin overlying the affected joints and may ulcerate and discharge pus containing C. immitis. Roentgen changes may mimic those of tuberculous arthritis, with destruction of cartilage and narrowing of joint spaces. There is little tendency toward production of bone in early lesions of the chronic form of the disease. The authors point out that whereas tuberculosis often attacks the joints directly, coccidiodal granuloma does so by extension from adjacent osseous lesions and that the latter more often affect multiple joints. This disease should be suspected in residents of or visitors in local endemic areas complaining of chronic progressive arthritis and in the presence of evidence of rapid progress of a destructive process in bone. No therapy has been of specific value for the chronic phase of this disease. Studies thus far reveal that sulfanilamide is not effective against this fungus.

An excellent article on the coccidioidal infections of bone by Benninghoven and Miller [297] reviews the subject of coccidioidal infection, about 500 cases of which have been reported to the California State Department of Health during the last forty years.

The disease is produced by the fungus Oidium coccidioides, which is usually found in the soil, and the adult form contains endospores which produce nodules

297. Benninghoven, D., and Miller, E. R.: Coccidioidal Infection in Bone, Radiology **38:** 663-666 (June) 1942.

closely resembling those of tuberculosis. Males are affected four times as frequently as females, probably because persons engaged in ranching and fruit picking, in which contact with the soil is close, are most frequently affected. The cases usually originate in the middle and southern parts of California. The portal of entry is the respiratory tract, the patient clinically having a mild influenza which may or may not be associated with erythema nodosum. In this primary phase a roentgenogram of the chest shows a small pneumonic focus with adenopathy resembling that of the primary phase of tuberculosis. In this phase the patient has a positive cutaneous allergic response to coccidioidin. All patients recover from the primary infection within a few weeks. Reinfection may induce the disease in its secondary or chronic granulomatous phase. Fortunately the secondary phase develops in only a small percentage of the patients. After the secondary focus is established either in the lungs or in the skin, metastatic foci may appear in the soft tissues, bones or parenchymal organs, and miliary dissemination is the terminal manifestation, dissemination being by the blood and lymph streams.

There are several commonly encountered types of osseous lesions found in this disease which may closely resemble tuberculosis of the bones or joints. Unilocular and multilocular cystlike areas, marginal erosions and destructive lesions with periosteal formation of new bone and abscesses of the soft tissues may develop. These lesions may go on to an advanced stage, giving rise to destruction with periosteal formation of new bone surrounding infected soft tissue, but sequestration, either with or without articular involvement, is rare. There is another type frequently seen in the short bones of the hand or feet or even in the shaft of a long bone showing widespread destruction. The articular involvement may be of two distinctly different types—the purely synovial or the synovial with subarticular destruction, which is indistinguishable from tuberculosis. Here there are capsular swelling and extensive periarticular osteoporosis, with cartilage and subarticular destruction of bone on both sides of the joint.

A multiplicity of lesions is the rule, and the bones most frequently involved are those of the spine, pelvis, hands and feet and the bones adjacent to the knee and ankle. No bones are exempt, though the diaphysial lesions are rare except in the short bones of the hands and feet. Coccidioidosis frequently may be indistinguishable clinically and roentgenographically from Pott's disease. The epiphysial cartilage, however, does not act as a barrier to the spread of the infection. Synovial infection may remain limited entirely to the synovium. Abscesses of the soft tissues are common. They may arise as primary lesions without involvement of bone, or they may extend to the underlying bone and involve it.

The prognosis of this disease in the secondary phase is grave, and the authors state that there is a mortality of approximately 60 per cent.

[Ed. Note.—These excellent papers on a disease whose secondary phase may so closely resemble tuberculosis are of extreme practical interest. While most cases seem to originate in the middle and southern parts of California, any condition that so closely resembles osseous tuberculosis must be watched for in other localities. The multiplicity of lesions so frequently found and the high mortality are, however, somewhat different from the manifestations of the infections with acid-fast organisms.]

Gajzágó and Göttche [298] describe 6 cases of infections with Salmonella suipestifer in children. Human infection with S. suipestifer was observed first during World

298. Gajzágó, D., and Göttche, O.: Suipestifer-Infektionen im Kindesalter, Monatschr. f. Kinderh. **88**:166-185, 1941; Salmonella Suipestifer Infections in Childhood, Am. J. Dis. Child. **63**:15-29 (Jan.) 1942.

War I, when it occurred in epidemic form. Subsequently infections attributed to food (raw milk, puddings, ice cream) were reported. The clinical picture resembled that of typhoid or dysentery. Later also sporadic cases were reported, and it was noted that the infection might appear in manifold forms such as pneumonia, pyelocystitis, cholecystitis, meningitis and endopericarditis, as well as in the forms resembling typhoid and dysentery. S. suipestifer has been isolated from abscesses of the liver, abscesses in uterine myoma and pyosalpinx.

In adults the condition is serious. In 19 of the 31 sporadic cases in which it has occurred in adults it has been fatal, but possibly the milder forms of the disease have not been recognized. In all, 28 cases of this infection in children have been reported. Fourteen cases have been reported in the United States, 10 of which were from Baltimore. The disease is more benign in children, the mortality rate being only 6 per cent. In 17 of 34 cases the organism caused an osteomyelitis. All osseous lesions were in infants under 2 years of age. In children over 2 years of age osteomyelitis did not occur. All of the 6 infants reported on by the present writers showed osteomyelitis.

Clinically, roentgenologically and pathologically this type of osteomyelitis is relatively benign. Incision was necessary in only 1 case. There may be multiple osseous foci and recurrences. The internal organs are not involved, and there is no anemia. The roentgen changes are very slight and become manifest in the fourth to the sixth week. Most of the foci appear in the proximal metaphysis of the humerus, i. e. in the shoulder region, or in the distal metaphysis of the femur, i. e. in the knee region. Slight inflammatory symptoms in these regions should rouse suspicion of infection with S. suipestifer. When suppuration is present, the organism can be isolated from the pus. The agglutination test gave a positive result in considerable dilution in all cases. In 2 of the 34 cases other organisms besides S. suipestifer were present. Most of the children were from poor country districts. In 1 case a hog dealer who had lost several hogs from infection lived in the house. Since some of the children were breast fed, it seems hardly possible that they had become infected from the hogs. The organism exists in the intestine of 10 per cent of normal swine. It seems probable that in epidemics of infection from food the latter was infected by food handlers, as carriers have been detected. The lower resistance of infants renders them susceptible to infection which does not attack their parents or the older children in the family. The infection is much more common than is supposed.

Localization of Infections.—Garlock [299] reports that in a previous series of 42 infections of tendon sheaths of the hand, only 14 per cent of the patients had restoration of normal function. He concludes that three factors determine the results: (1) the duration of the disease before treatment (if it is over twenty-four hours there is little chance of survival of the involved tendons); (2) the degree of tension within the sheath, with its direct influence on the precarious blood supply to the tendons; (3) the introduction of secondary contaminant organisms after open drainage of the flexor sheaths, causing necrosis; (4) the virulence of the infecting organism and the resistance of the host.

On these premises he advises the following treatment: 1. If the infection is of less than twenty-four hours' duration, aspirate the tendon sheath as completely as possible. 2. Make smears and cultures of the aspirated material. 3. Administer sulfonamide compounds at once—preferably intravenously. 4. If there are only moderate tension and swelling in the sheath, immobilize the digit in partial flexion

299. Garlock, J. H.: Suppurative Tenosynovitis of Hand: Plan of Treatment, J. Mt. Sinai Hosp. **8**:540-542 (Jan.-Feb.) 1942.

and use hot soaks if desired. 5. If there are great tension and swelling, make lateral incisions in a bloodless field, with multiple small incisions in the tendon sheath. Do not use a drain. 6. Apply a light dressing and immobilize the finger in partial flexion with a sterile metal splint. Wrap the hand and forearm in sterile towels. Leave the dressings on for three or four days and continue treatment with a sulfonamide compound. 7. Start early active motion. The author reports 5 cases in which the patients were treated by this method. In 4 cases hemolytic streptococci were the infecting organisms, and in 1 case it was Staphylococcus aureus. The fingers infected with streptococci were all restored to complete function. The patient with staphylococcic infection had a serviceable digit with slight limitation of flexion.

Chont [300] points out that the commonest causative agents of suppurative arthritis of the hip in children under the age of 2 are the streptococcus and the meningococcus. In older children the offending organism is usually the staphylococcus. The gonococcus may be the causative agent at any age.

Since the infection is blood borne, there are symptoms of toxemia. Local signs are pain, swelling and impaired function of the hip. These signs and symptoms occur also with periarthritis, toxic reaction of the joint, nonpurulent synovitis and osteomyelitis. Roentgen examination helps to differentiate suppurative arthritis of the hip from osteomyelitis.

Suppurative arthritis of the hip begins with an increased secretion of serum into the joint cavity, which produces an increased intracapsular pressure. A lateral and upward subluxation or dislocation of the head of the femur occurs. Later the synovial fluid becomes purulent and destroys cartilage, so that fusion or pathologic dislocation results. This lateral and upward displacement of the head of the femur as demonstrated by the roentgenogram is pathognomonic of early infectious arthritis of the infantile hip. Cases are reported to demonstrate this condition.

Aranow and Wood [301] review the causes of scarlet fever and point out that different strains of beta hemolytic streptococci may produce antigenically different toxins which cause scarlet fever, but are not neutralized by the standard Dick antitoxin. The purpose of the paper is to report a case with immunologic experiments which suggests that scarlet fever may be caused by staphylococcus toxin.

The case is that of a 15 year old girl who was admitted to the hospital with a history of pain in the left thigh and fever for four days. She was acutely ill, with a temperature of 105 F., and had the typical manifestations of scarlet fever (rash, glossitis, etc.), associated with tenderness over the lateral aspect of the thigh.

Repeated cultures of the blood showed a hemolytic strain of Staph. aureus. Rash and fever responded to scarlet fever antitoxin. Pain and tenderness became localized over the greater trochanter. It was incised and drilled, and pus containing hemolytic Staph. aureus was encountered. Treatment with sulfadiazine resulted in continued improvement.

Repeated search revealed no evidence of beta hemolytic streptococci in this case. Experiments carried out on the strain of hemolytic Staph. aureus found in the pus showed that filtrable erythrogenic toxin was produced. This toxin was neutralized by commercial scarlatinal antitoxin.

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300. Chont, L. K.: Roentgen Sign of Early Suppurative Arthritis of Hip in Infancy, Radiology **38**:708-714 (June) 1942.

301. Aranow, H., Jr., and Wood, W. B., Jr.: Staphylococcic Infection Simulating Scarlet Fever, J. A. M. A. **119**:1491-1495 (Aug. 29) 1942.

Schein [302] reports an unusual complication following the plating of a fractured femur with a long vanadium steel plate. About six months after the plate was applied the patient had a sudden attack of severe pain in the right thigh, without any history of preceding injury or illness, and his temperature rose to 105 F. The wound was opened widely, and the discolored Lane plate was exposed and removed. The plate had become very loose and was bathed in greenish gray pus, from which Salmonella typhimurium was cultured. The wound was treated by the Orr method and finally healed without further infection of the bone. The author is convinced that the infection was not a primary osteomyelitis but that it originated from the material that had accumulated about the plate and screws.

The author states that at the Mount Sinai Hospital plates are usually left in situ but that it has been found necessary to remove more than 5 per cent from their plated fractures when the older type of Sherman vanadium steel plate was used.

[Ed. Note.—The isolation of one of the paratyphoid group of organisms, as well as the fortunate outcome of the case presented, is of interest.]

Goldenberg [303] reports the case of an 11 year old boy whose illness was misdiagnosed as cellulitis of the left leg on the fifth day and later was proved to be osteomyelitis of the fibula. He was given expectant treatment entirely (i. e. dextrose in saline solution intravenously and hot, wet magnesium sulfate dressings), and sulfonamide compounds were not used. On the twelfth day the leg was immobilized in a circular plaster bandage. Support was continued for a period of eight months, during the latter part of which weight bearing was permitted. Periodic roentgenograms showed progressive destruction of the proximal 4 inches (10 cm.) of the fibula with subsequent reformation of the shaft, beginning in the distal part. Three years and two months later there was no roentgen evidence of active disease or sequestrum formation, and complete regeneration of the fibula had taken place.

[Ed. Note.—The clinical aspects are minimized in this report, and no mention is made of an etiologic agent. It is not recorded whether blood cultures and other laboratory studies were made, though they would be of interest.]

Guthrie [304] describes the case of a 7 month old boy with initial symptoms of an infection of the upper respiratory tract followed by arthritis of the right shoulder. Bronchopneumonia developed followed by nuchal rigidity. A lumbar puncture showed slight increase of pressure but otherwise revealed nothing. Autopsy disclosed suppurative periarthritis of the right shoulder without involvement of the joint, pus in the bronchioles, patchy bronchopneumonia of the suppurative type and bilateral otitis media. There was no evidence of meningitis. Bacteriologic, serologic and biologic studies identified the infecting organism as S. suipestifer, var. Kunzendorf.

In reviewing the literature he found that Salmonella infections in early childhood tend to produce bacteremia and foci of suppuration in organs and tissues. S. suipestifer may produce lesions in bones and joints, and in 20 per cent of 71 cases of this infection involving the skeletal system septic arthritis was the predominant lesion. Pulmonary complications frequently accompany lesions elsewhere. The

302. Schein, A. J.: Late Infection of Healed Lane-Plated Fracture of Femur by Salmonella Typhimurium: Lane Plate as Locus Minoris Resistentiae, J. Mt. Sinai Hosp. **9**:154-159 (Sept.-Oct.) 1942.

303. Goldenberg, R. R.: Roentgenographic Study of Acute Osteomyelitis of Fibula Treated Conservatively, J. Bone & Joint Surg. **24**:447-451 (April) 1942.

304. Guthrie, K. J.: Suppurative Periarthritis in Infant Due to Suipestifer Bacillus, Arch. Dis. Childhood **16**:269-274 (Dec.) 1941.

portal of entry is probably the gastrointestinal tract, but pathologic changes are not usually found there and the organism can rarely be isolated from feces. Blood cultures are often positive. The organism can also enter via the rhinopharyngeal portal. Infection by the latter route accounts for the aural and pulmonic involvement in the case cited.

[ED. NOTE.—The author makes no mention of treatment.]

Kirby-Smith [305] reports 1 case of osteomyelitis of the patella and states that he has found only 60 reported in the literature. In his case the infection was treated by excising a portion of the patella and draining the wound. When last seen about two years after operation, the patient presented approximately normal return of active function to the joint, and the roentgenograms taken at intervals showed that about ten and a half months after operation the patella had regenerated, although it was rather irregular in outline.

According to McMaster,[306] typhoid spine is a rare complication of generalized typhoid infection. In one series of 410 patients only 1 had spinal involvement. The diagnosis of typhoid spine is usually based on the history plus a Widal test. A negative result of the test, however, does not exclude this disease. The physical manifestations include tenderness, muscular spasm, limitation of motion and occasionally scoliosis and kyphosis. By roentgen examination the process can usually be localized to two vertebrae in the lower thoracic or lumbar region. There is narrowing or absence of the intervertebral disks with osteitis of the adjacent vertebral bodies, which themselves may be only slightly invaded. Ossification of the periosteal and perispinal ligaments may produce bridging. Abscesses are rare. In making the differential diagnosis coccidioidal granuloma and brucella spondylitis should be considered. Typhoid organisms may be found in the vertebral marrow many years after generalized infection. The treatment consists of immobilization by means of a plaster cast or a brace. A spinal fusion is indicated if the patient has recurrent attacks of pain in the back with prolonged disability, unless there are serious systemic lesions present.

The author reports 4 cases, in 3 of which the disease was diagnosed five or more years after subsidence of the acute infection. In 2 cases spinal fusion was performed with apparent cure.

Stone [307] reviews the literature on osteomyelitis of the long bones in the newborn and reports 4 new cases. He concludes that the disease is relatively benign, with a favorable prognosis. In 63 per cent of the infants in one series the etiologic agent was a streptococcus. In those under 6 months of age the mortality was 44 per cent. When recovery takes place the wounds heal rapidly after drainage, sequestration is rare and recurrences are extremely infrequent. Often a study of end results reveals that the site of the original lesion is roentgenographically invisible. The involucrum is visible much sooner than in older children and usually involves one-half the length of the bone. If the infant survives the acute phase, the disease is of relatively short duration and the prognosis of the osseous lesion is excellent. A minimal amount of surgical intervention is adequate. Drainage is necessary only if there is a palpable mass, and the bone should be left untouched if a secondary abscess can be adequately drained. When the Orr technic was used in treatment healing usually occurred in four to eight weeks.

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305. Kirby-Smith, H. T.: Acute Osteomyelitis of Patella: Case Report, J. Bone & Joint Surg. **24**:942-944 (Oct.) 1942.

306. McMaster, P. E.: Typhoid Spine, U. S. Nav. M. Bull. **40**:957-963 (Oct.) 1942.

307. Stone, S.: Osteomyelitis of Long Bones in Newborn, Am. J. Dis. Child. **64**:680-688 (Oct.) 1942.

When osteomyelitis is associated with septicemia or secondary to umbilical sepsis, the prognosis is more grave. Sepsis, not osteomyelitis, kills.

The author reports on 4 cases of osteomyelitis involving long bones. In 1 the infecting organism was Streptococcus viridans, and in 3 it was Staphylococcus aureus. All the patients recovered, and none had septicemia or appeared acutely ill. They were admitted to the hospital because of localized swellings of the extremities or diminished motion of the arms and legs.

He explains the benign nature of the disease on the basis of the anatomy of the bone of the newborn, which has large vascular spaces and is less rigid than that of adults. The cortical bone is thin, especially at the metaphysis, so that there is freer communication between the marrow and the subperiosteal spaces and escape of pus is easier.

Value of Chemotherapy.—The report on the use of cod liver oil ointment by Aldrich [308] stimulated Wolferman and Adams [309] to make up an ointment consisting of white wax, standard cod liver oil and sulfathiazole or sulfanilamide. They believe that the addition of either sulfonamide compound will compensate for the deficiency in bacteriostatic power of the cod liver oil ointment and render it useful both as an adjunct to the Orr method of treating chronic osteomyelitis and as a local application to extensive abrasions and superficial burns. These authors also feel that the use of fine-meshed old sheeting or linen, which has practically no interstices, is a definite factor in promoting healing in wounds. They have found that a mixture of 40 per cent white wax and 60 per cent cod liver oil is satisfactory. The wax is melted over a Bunsen burner, and then standard cod liver oil is added. By rapid stirring and continued heating, lumping can be prevented. The mixture is then cooked for at least an hour and a half and allowed to cool. Enough sulfathiazole or sulfanilamide is then added to make 6 per cent ointment. When the ointment has been autoclaved it is ready for use. These authors' experience with this ointment is limited as yet, but they believe there is sufficient evidence to permit recommending it to others for trial.

[ED. NOTE.—Finely meshed material and the simple preparation the authors describe appeal to the editors as worthy of further trial in the hands of other observers. One of the disadvantages of loose mesh gauze is that the loose strands that become embedded in the wound are difficult to remove at times. Any practical modification of the valuable Orr treatment is worthy of a trial in other clinics.]

Cantor [310] reports 1 case of chronic osteomyelitis treated by sprinkling sulfanilamide powder into the wound and covering it with antipeol ointment. This, in the author's opinion, stimulated this wound to a remarkable degree. The antivirus, "antipeol," is prepared from sterile filtrates of Staphylococcus aureus, Staph. albus and Staph. citreus, Streptococcus pyogenes, Str. viridans and Str. hemolyticus, and Bacillus pyocyaneus and is mixed with a base of hydrous wool fat containing zinc oxide, ichthammol (ammonium sulfoichthyolate) and sodium borate. The author points out that this antivirus does not have an actual bactericidal effect but that it prevents the development of the bacteria, thus bringing growth to a standstill.

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308. Aldrich, R. H.: Cod Liver Oil Ointment in Surgery: Eight-Year Study, Indust. Med. **11**:153-157 (April) 1942.

309. Wolferman, S. J., and Adams, W. F.: Cod Liver Oil Ointment with Sulfonamides in Wounds and Osteomyelitis, Indust. Med. **11**:318-319 (July) 1942.

310. Cantor, I. B.: Osteomyelitis: Report of Case, J. M. A. Georgia **31**:249-250 (June) 1942.

The clinical use of penicillin is discussed by Herrell and his associates.[311] The authors state that, while this highly soluble drug may be given by mouth, care must be taken to introduce the material into the duodenum, and they are of the opinion that continuous or nearly continuous intravenous administration is the method of choice at present. These authors suggest that the only method of identifying the material in the tissues and in the urine is by means of a biologic test and that because of the limited amount of penicillin available only 4 of their patients have received it. In all of these the organism was Staph. aureus, and the outcome was strikingly satisfactory.

They report a case in which penicillin was used on a white man 33 years of age who was admitted to the hospital because of marked cellulitis of the nose and edema of the right eyelid and of the right side of the face and neck. The submaxillary glands on the right were enlarged and tender, and his temperature on admission was 104 F. Diagnosis of extensive cellulitis of the face and orbit was made, and the possibility of a cavernous sinus thrombosis was considered. The patient had a positive blood culture of Staph. aureus as well as a positive culture of the same organism from the right nasal passage. Penicillin was administered intravenously after the unsatisfactory course during the first twenty-six hours when sulfadiazine was used. Penicillin was administered at the rate of 25 to 30 drops a minute of a solution in which 115 mg. of penicillin was dissolved in a liter of isotonic solution of sodium chloride. A blood culture made twenty-two hours after the beginning of this treatment was sterile, and two hours later the patient's temperature was 100 F. At no time was there evidence of toxicity which might be attributed to the use of penicillin, and the temperature returned to normal and stayed there after seven days. The patient recovered.

[ED. NOTE.—This is a drug that one will doubtless hear a great deal more about in the future, for it would seem to be amazingly useful in treatment of infection due to Staph. aureus. The technical difficulties in preparing the material plus its use by the armed forces have to a great degree retarded widespread clinical use of penicillin in civil practice.]

The introduction of Blaisdell and Harmon's[312] article on suppurative disease of the joints deals with the historical aspect of its treatment. They stress the important contributions of Hibbs, who contended that pus within a joint was a main factor in the destruction of cartilage and that to lessen this damage surgical drainage of the joint was necessary, and Phemister, who demonstrated the destructive element in pus which destroyed cartilage and established the fact that pressure in the presence of a pyogenic exudate accelerated the erosion of cartilage. The modern trend of treatment has been toward conservatism, and roentgen visualization has enabled the surgeon to be directed intelligently toward diagnosis and treatment of osseous suppuration. Until the recent advent of chemotherapy, few contributions of major importance followed those of Phemister. However, the authors feel that the quality of treatment has steadily improved, and with it the end results.

They state:

The purpose of this paper is to emphasize the need for early and prompt bacteriological diganosis by joint aspiration and vigorous and meticulous therapy including the prolonged

311. Herrell, W. E.; Heilman, D. H., and Williams, H. L.: The Clinical Use of Penicillin, Proc. Staff Meet., Mayo Clin. **17**:609-616 (Dec. 30) 1942.

312. Blaisdell, J., and Harmon, P. H.: Suppurative Joint Disease and Its Relation to Pyogenic Osteomyelitis: Review of End Results of Sixty-Seven Involved Joints in Fifty-Seven Patients; Modern Chemotherapeusis, Surg., Gynec. & Obst. **74**:796-808 (April) 1942.

application of traction to the involved extremity and to describe the application of specific chemotherapy, both during the acute stage and as used to heal the wound. The employment of traction results in a greater percentage of movable joints in the end-results.

The patient with suppurative articular disease presents himself with a painful, swollen, and immobile joint, splinted by spasm of neighboring muscles. Symptoms and findings of acute or subacute infection are present. The chief conditions considered in the differential diagnosis are: acute rheumatic fever; sympathetic sterile effusion in the joint produced by trauma or neighboring infection; intermittent hydroarthrosis, articular tuberculosis (the acuteness of suppurative articular disease usually prevents confusion); hemophilia; traumatic hemarthrosis; acute rheumatoid arthritis; acute bursitis, periarticular cellulitis, and small fractures and sprains. In deep lying joints, the local extension in the joint may be masked by pain and muscular spasm; therefore, the presence of pus within the joint can be determined only by aspiration. This procedure is further indicated at the earliest possible moment for obtaining material for smears and cultures, as well as being the first step in treatment, since suppurative products should not be allowed to accumulate. Roentgen examination of the part should be made immediately. No osseous alterations can be expected prior to seven to fourteen days after onset; however, an early roentgenogram enables the surgeon to rule out preexisting disease of the bone. The earliest finding is that of narrowing of the joint space, and for this reason a roentgenogram of the corresponding joint should be taken.

The treatment of acute suppurative articular disease should be designed to preserve motion if possible and to relieve pain and minimize damage to the joint by aspiration (or arthrotomy if indicated) and traction. Chemotherapy aids in controlling suppuration and in sterilizing the blood stream when involved. The necessity of early diagnosis by joint aspiration and bacterial culture and smear is stressed, since the proper chemotherapeutic agent is selected on the basis of the results from bacterial culture and smear. When this information is lacking during the first few hours, the agents that are active against hemolytic Staph. aureus (sulfathiazole and sulfadiazine) are to be used presumptively. For children who have acute articular complications following infection of the upper respiratory tract and of the middle ear, sulfanilamide is to be used.

Two cases are reported, in 1 of which the patient was treated successfully for suppurative disease of the left knee (with foreign body) by aspiration, traction, sulfathiazole and arthrotomy to permit removal of the foreign body and facilitate drainage. Drains which were inserted at the time of arthrotomy were removed on the fifth postoperative day, and on the twenty-third postoperative day the wound was healed and has remained so without recurrence of symptoms. (This was a case uncomplicated by osteomyelitis.) The second case is that of a 26 year old man with a history of osteomyelitis of the distal portion of the right femur of twelve years' duration, with extension of the process to involve the right knee. In spite of chemotherapy and traction, pain on motion of the affected joint persisted, and because of the extensive involvement of the femur pathologic fracture was feared. A long leg cast was therefore applied.

As a result of determination of the concentration of sulfathiazole in the blood and the knee joints of patients who presented sterile effusions in which the concentration of the drug in the aspirated joint fluid was found to be approximately two thirds of that present in the blood, the authors feel that perhaps an increasing number of primary operations can be performed on chronic suppurative joints without danger of sinuses developing when sulfonamide drugs are used both locally and by mouth after operation. They state that the restrictions in operating on bone

which was formerly the seat of infection can be relaxed if local and systemic chemotherapy is utilized. However, the limitations associated with this new auxiliary are not as yet defined and are still under investigation.

[ED. NOTE.—This article is well illustrated and is a review of 67 involved joints in 57 patients. From these data, the most frequently involved joints by suppuration were found to be, in the order named: hip, knee, ankle, shoulder, elbow and wrist.]

Toumey [313] discusses the treatment of chronic osteomyelitis with sinus formation. He has found the following plan most effective:

1. Oral chemotherapy is begun one week preceding operation. He uses either sulfathiazole or sulfadiazine, taking the usual precautions. Four grams is given initially, followed by 1 Gm. every four hours.

2. At operation débridement and saucerization are carried out. Four to 10 Gm. of sulfathiazole is dusted into the layers of the wound as it is closed. A plaster cast is then applied.

3. Oral chemotherapy is continued for a week. Two cases are reported, in which the infection remained healed after nine months and five months respectively.

McKeown [314] makes a preliminary report of 6 unselected consecutive cases of osteomyelitis in children from 9 to 14 years of age. Three patients were boys, and 3 were girls. The surgical treatment was minimal. It consisted of incision of the periosteum and drilling of the bone in the acute stage of the disease and sequestrectomy done later if needed. The dose of sulfathiazole was 1 Gm. per 20 pounds (9.1 Kg.) of body weight. The patients were divided into two groups. The patients in group 1 were given the drug at the onset of the disease. Administration was continued for eight days, followed by an interval of three weeks, after which the treatment was repeated if necessary. The patients in group II were given the drug twelve to forty-eight days after the onset of the disease, and the dose was repeated as required. In the latter group operation was performed before sulfathiazole was given. In 2 cases of each group Staph. aureus was the etiologic agent. Only one blood culture was made and that was negative. The osteomyelitis occurred in the femur in 4 cases, in the tibia in 1 case and in the humerus in 1 case. Plaster of paris was applied in the cases of 3 of the patients, all in group I. Petrolatum gauze packing was used for 2 patients of group I.

The author reached the following conclusions:

1. In no patient was there spreading and gross involvement of bone.

2. In group I the total bony involvement was minimal; in group II the bony change was more marked.

3. Duration of treatment for group I was five months; for group II it was eleven months.

4. Duration of treatment was one half of the average of the previous five years, when sulfathiazole was not in use.

[ED. NOTE.—1. There was no uniformity of studies (blood cultures or determinations of blood sulfathiazole levels or of etiologic agents). 2. In the description of group II there was nothing to indicate whether plaster of paris or petrolatum gauze was or was not used. Hence comparison of the results from early and from late administration of sulfathiazole is not complete, since the other factors were not controlled.]

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313. Toumey, J. W.: Chemotherapy in Osteomyelitis, Lahey Clin. Bull. **3**:12-16 (July) 1942.

314. McKeown, K. C.: Conservative Treatment of Osteomyelitis, Proc. Roy. Soc. Med. **35**:215-217 (Jan.) 1942.

Wilensky [315] discusses the value of chemotherapy in the treatment of osteomyelitis, giving a résumé of the technical information with comments on the general phenomena involving the body as a whole and the local phenomena involving any particular area, tissue or organ of the body. In the acute hematogenous osteomyelitis he feels that the only stage in which any chemotherapeutic, bacteriostatic or bacteriocidal effect is to be expected from chemotherapy is when bacteremia is present. He points out that should additional numbers of bacteria be continuously shed into the blood stream from an infected blood clot, chemotherapy will have no apparent effect on the positive blood cultures. It will not have a lasting effect unless all local lesions which may produce bacteremia have been thoroughly removed by surgical means.

He feels that the use of sulfonamide compounds may have a definite place as a prophylactic and advises preparing certain classes of patients preoperatively to eliminate certain postoperative reactions and infections. He cites the methods by which sulfanilamide, sulfapyridine, sulfathiazole and sodium sulfapyridine can be administered and feels that all of these drugs act by inhibiting the biologic activities of the bacteria but that the actual destruction of bacteriolysins is accomplished by the ordinary antibacterial agencies of the body. The sulfonamide compounds act only by intimate contact with the offending bacteria and not when the bacteria are locked away out of ready contact with the circulating body fluid. The results are not always predictable under the best of circumstances, and he feels that treatment of osteomyelitis with sulfanilamide and its derivatives has not produced the startling results noted in certain other conditions, especially pneumonia. Sometimes the beneficent results have occurred spontaneously, and for the present, a final evaluation of the value of the sulfonamide compounds in treating osteomyelitis must be guarded.

[ED. NOTE.—This long article clearly points out some of the limitations of the use of sulfonamide compounds, but the author apparently is rather pessimistic about the beneficent results obtained in both acute and chronic osteomyelitis unless there are both an accompanying bacteremia and adequate surgical intervention. It is interesting to recall the enthusiastic acceptance accorded the local and systemic use of sulfonamide compounds in acute war injuries. To date success has been greater in certain medical conditions, though the mounting favorable statistics on the local therapy of war wounds are striking.]

Infection of Muscles.—Cockrell [316] describes a condition that in the eastern tropics is called myositis purulenta tropica. It is an inflammation of the muscles, which is usually acute and of bacterial origin with signs of acute infection. The lesions may be single or multiple. The cause is most often infection with Staph. aureus, streptococci, Escherichia coli or a combination of the three. In 25 per cent of the cases there is preexisting pulmonary infection. The muscles show hyaline, granular or fatty degeneration. The disease occurs in persons of all ages and of both sexes, but more frequently in males than in females. The onset is sudden and resembles that of pyemia or septicemia. When localized, the swelling has a board-like consistency until suppuration occurs, as it usually does in one or two weeks. It is hard to diagnose and is often confused with appendicitis, hematoma, perinephric abscess, tuberculosis of the hip or spine, psoas abscess (tuberculosis), trichinosis, filariasis, parasitic infections, bruises, injuries and insect bites. The

315. Wilensky, O.: Value of Chemotherapy in Treatment of Osteomyelitis, Arch. Surg. **44**:234-259 (Feb.) 1942.

316. Cockrell, B. A.: Primary Suppurative Myositis, M. Bull. Vet. Admin. **19**:171-177 (Oct.) 1942.

treatment, in general, is supportive. Other forms of therapy include the administration of sulfonamide compounds, local application of hot wet dressings and surgical drainage instituted as soon as indicated. Every effort should be made to avoid contractures and muscular atrophy.

The author reviews 133 cases, most of which were from the South Pacific, although 25 occurred in the United States. In many of the cases the disease was probably misdiagnosed as cellulitis, abscess or psoas abscess of tuberculous origin.

Goldman [317] states that inflammatory lesions of muscles are rare and are usually classified as (1) primary suppurative myositis, (2) dermatomyositis, (3) neuromyositis, (4) primary myositis fibrosa and (5) progressive myositis ossificans.

He reports the case of a 63 year old Jew. At onset there was a cracking, vesiculated and keratotic eruption on the hands and between the toes. This improved after treatment with a salicylic acid ointment. The next sign noted was puffiness of the hands and face. Physical examination revealed early lenticular opacities of both eyes but otherwise nothing abnormal. The results of laboratory studies were essentially normal. One year later there were swelling and dermatitis of the hands and feet with an occasional generalized eruption, which was thought to be due to a fungous infection. Stiffness and pain in the right leg developed later and were followed by swelling of the fingers. An electrocardiogram showed low voltage in all leads and an inverted T wave in lead I. Thyroid was given without effect. Pain in the arms continued, and four months after his third examination there was sudden onset of generalized muscular weakness and acute difficulty in swallowing and phonation. The impression was that of atypical bulbar palsy with no fibrillary tremors. There were wasting of muscles, weakness of the pharyngeal muscles and diminished vibratory sense. The clinical impression was that the patient had polyneuritis and myasthenia. Intravenous administration of thiamine hydrochloride and prostigmine bromide resulted in some improvement in vibratory sense, but dysphagia increased and the patient died.

At autopsy the skin was clear. There were atrophy and paleness of the cervical and trunk muscles. There were milk spots on the epicardium, and the spleen was small and fibrotic. The cranial bones were softer than normal. There was slight congestion over the cerebral cortex. The skeletal muscles showed hyaline degeneration with infiltration of lymphocytes, monocytes and polymorphonuclear cells. There was also generalized arteriosclerosis with extreme malnutrition. The neuropathologic diagnosis was "chronic cell change" in the medulla and the cerebral cortex.

The author believes that the early cutaneous lesions are indicative of dermatomyositis and refers to a similar condition reported by Hendry and Anderson in which cutaneous changes antedated involvement of muscles. He calls this a case of polymyositis and says that one or more biopsies of skin and muscle should have been done early in the study.

(To Be Continued)

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317. Goldman, D.: Polymyositis: Report of Fatal Case, Arch. Int. Med. **70**:822-828 (Nov.) 1942.

Special Notes

SECTION ON SURGERY, GENERAL AND ABDOMINAL, OF AMERICAN MEDICAL ASSOCIATION

Applications for places on the program of the Section on Surgery, General and Abdominal, for the next Annual Session, to be held in Chicago, June 12 to 16, 1944, are now being received. All Fellows of the American Medical Association are eligible. Essayists who are not Fellows may be accepted by invitation. Applications should be addressed to Dr. Alton Ochsner, 1430 Tulane Avenue, New Orleans 13.

Because of the lateness of this announcement, the closing date for applications has been extended to December 31.

CORRECTION

In the article by Dr. D. J. Leithauser entitled "Confinement to Bed for Only Twenty-Four Hours After Operation: A Means of Preventing Pulmonary and Circulatory Complications and of Shortening the Period of Convalescence," in the August issue (ARCH. SURG. **47**:203, 1943), the second word of the ninth line in the report of case 10, on page 213, should be "thirtieth" instead of "thirteenth."